BIRLA CENTRAL LIBRARY
PILANI (Rajasthan)
Class No. 547.06
Book No. M31H
Accession No. 64058

THE HETEROCYCLIC DERIVATIVES
OF PHOSPHORUS, ARSENIC, ANTIMONY, BISMUTH, AND SILICON

THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

A SERIES OF MONOGRAPHS

ARNOLD WEISSBERGER, *Consulting Editor*

The Heterocyclic Derivatives of PHOSPHORUS, ARSENIC, ANTIMONY, BISMUTH, and SILICON

FREDERICK GEORGE MANN
Cambridge University, England

1950
INTERSCIENCE PUBLISHERS, INC., NEW YORK
INTERSCIENCE PUBLISHERS LTD., LONDON

Copyright, 1950, Interscience Publishers, Inc.

ALL RIGHTS RESERVED. This book or any part thereof must not be reproduced without permission of the publisher in writing. This applies specifically to photostat and microfilm reproductions.

INTERSCIENCE PUBLISHERS, Inc., 215 Fourth Ave., New York 3, N. Y.

For Great Britain and Northern Ireland:

Interscience Publishers Ltd., 2a Southampton Row, London W. C. 1

PRINTED IN THE UNITED STATES OF AMERICA BY MACK PRINTING CO., EASTON, PA.

INTRODUCTION TO THE SERIES

The Chemistry of Heterocyclic Compounds

The chemistry of heterocyclic compounds is one of the most complex branches of organic chemistry. It is equally interesting for its theoretical implications, for the diversity of its synthetic procedures, and for the physiological and industrial significance of heterocyclic compounds.

A field of such importance and intrinsic difficulty should be made as readily accessible as possible, and the lack of a modern detailed and comprehensive presentation of heterocyclic chemistry is therefore keenly felt. It is the intention of the present series to fill this gap by expert presentations of the various branches of heterocyclic chemistry. The subdivisions have been designed to cover the field in its entirety by monographs which reflect the importance and the interrelations of the various compounds, and accommodate the specific interests of the authors.

ARNOLD WEISSBERGER

Research Laboratories
Eastman Kodak Company
Rochester, New York

Contents

Foreword . . . 1

I. Heterocyclic Derivatives of Phosphorus . . . 9
- Five-Membered Ring Systems Containing Only Carbon and Phosphorus 9
  - Cyclotetramethylenephosphines . . . 9
- Six-Membered Ring Systems Containing Only Carbon and Phosphorus. 10
  - Cyclopentamethylenephosphines . . . 10
  - 1,2,3,4-Tetrahydroisophosphinolines . . . 10
- Four-Membered Ring Systems Containing Carbon, Phosphorus, and Oxygen . . . 13
- Five-Membered Ring Systems Containing Carbon, Phosphorus, and Nitrogen . . . 14
- Five-Membered Ring Systems Containing Carbon, Phosphorus, and Oxygen . . . 17
  - *o*-Phenylenechlorophosphonites . . . 17
- Six-Membered Ring Systems Containing Carbon, Phosphorus, and Nitrogen . . . 19
  - Phenphosphazines . . . 19
- Six-Membered Ring Systems Containing Carbon, Phosphorus, and Oxygen . . . 21
  - Salicylchlorophosphonite . . . 21
- Ten-Membered Ring Systems Containing Carbon, Phosphorus, and Oxygen . . . 22

II. Heterocyclic Derivatives of Arsenic . . . 25
- Five-Membered Ring Systems Containing Only Carbon and Arsenic . . . 25
  - Cyclotetramethylenearsines . . . 25
  - Arsindoles . . . 26
  - Arsindolines and Isoarsindolines . . . 30
  - Arsindolines . . . 30
  - Isoarsindolines . . . 31
  - Arsafluorenes or 2,3-Benzarsindoles . . . 36
- Six-Membered Ring Systems Containing Only Carbon and Arsenic . . . 38
  - Cyclopentamethylenearsines . . . 38
  - Tetrahydroarsinolines and Tetrahydroisoarsinolines . . . 42
  - 1,2,3,4-Tetrahydroarsinolines . . . 43
  - 1,2,3,4-Tetrahydroisoarsinolines . . . 45
  - Arsacridines . . . 49
  - Arsanthridines . . . 52
  - 2-Arsaperinaphthanes (or 2-Arsaperinaphthindanes) . . . 55

Seven-Membered Ring Systems Containing Only Carbon and Arsenic . . 57
- 6-Arsa-1,2,3,4-dibenzcyclohepta-1,3-dienes 57

Five-Membered Ring Systems Containing Carbon, Arsenic, and Oxygen 58
- Anhydrides of *o*-Carboxyphenyl Arsinous and Arsinic Acids 58
- *o*-Phenylenephenylarsonite 62
- Spirocyclic Esters of Glycols, *o*-Dihydroxybenzenes, and α-Hydroxycarboxylic Acids with Arsonic Acids 62
- Tripyrocatechylarsenic Acid 67

Five-Membered Ring Systems Containing Carbon, Arsenic, and Sulfur . 70
- 2-Arsa-1,3-dithiacyclopentanes 70

Five-Membered Ring Systems Containing Carbon, Oxygen, and Two Arsenic Atoms 75
- Anhydride of *o*-Phenylene-bisarsonous Chloride 75
- Anhydride of 5,10-Dihydroxy-5,10-dihydroarsanthrene 75

Five-Membered Ring Systems Containing Carbon, Palladium, and Two Arsenic Atoms 77

Six-Membered Ring Systems Containing Carbon, Arsenic, and Nitrogen 80
- Phenarsazines 80
- Azaphenarsazines 99

Six-Membered Ring Systems Containing Carbon, Arsenic, and Oxygen . 100
- Phenoxarsines 100

Six-Membered Ring Systems Containing Carbon, Arsenic, and Sulfur . 114
- Phenyl-thiarsine 114
- Phenthiarsine 114

Six-Membered Ring Systems Containing Carbon and Two Arsenic Atoms 116
- Ethylene-*o*-phenylenediarsine 116
- Arsanthrene and Its Derivatives 117
- Tri-*o*-phenylenediarsine 125

Seven-Membered Ring Systems Containing Carbon and Two Arsenic Atoms 127
- *o*-Phenylenetrimethylenediarsine 127

III. Heterocyclic Derivatives of Antimony 129

Five-Membered Ring Systems Containing Only Carbon and Antimony . 129
- Cyclotetramethylenestibines 129
- Stibinafluorenes 130

Six-Membered Ring Systems Containing Only Carbon and Antimony . . 134
- Cyclopentamethylenestibines 134
- Stibacridines 135

Five-Membered Ring Systems Containing Carbon, Antimony, and Oxygen 140
- Potassium Antimonyl Tartrate (Tartar Emetic) 140
- Derivatives of Pyrocatechol and Other 1,2-Dihydric Phenols 143

Five-Membered Ring Systems Containing Carbon, Antimony, and Sulfur........ 150
2-Stibina-1,3-dithiacyclopentanes........ 150
Five-Membered Ring Systems Containing Carbon, Antimony, Oxygen, and Sulfur........ 151
Antimony Derivatives of Thioglycollic Acid........ 151
Six-Membered Ring Systems Containing Carbon, Antimony, and Oxygen........ 152
Phenoxstibines........ 152
IV. **Heterocyclic Derivatives of Bismuth**........ 157
Six-Membered Ring Systems Containing Only Carbon and Bismuth.... 157
Cyclopentamethylenebismuthine........ 157
Five-Membered Ring Systems Containing Carbon, Bismuth, and Oxygen 158
Derivatives of Pyrocatechol and Other 1,2-Dihydric Phenols........ 158
V. **Heterocyclic Derivatives of Silicon**........ 161
Six-Membered Ring Systems Containing Only Carbon and Silicon ... 161
Cyclopentamethylenesilicon Derivatives........ 161

Index........ 163

Foreword

The object of this book is to give a systematic account of the heterocyclic organic derivatives of phosphorus, arsenic, antimony, and bismuth, that is to say, of those derivatives which contain these elements and carbon (with or without other elements) in the ring system. Compounds in which the ring is purely inorganic, *i.e.*, carbon-free, are not considered.

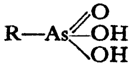
A glance at the Table of Contents will show the order in which the various ring systems are discussed. We may take the arsenic compounds as an example, since they are the most numerous. The first types to be discussed are those in which the ring consists solely of carbon atoms and one arsenic atom, the types being taken in order of increasing size of the ring. Therefore the cyclotetramethylenearsines come first, as five-membered ring compounds, followed by all those derivatives such as the arsindoles and isoarsindolines which contain the same ring system, that is to say, the ring with the same constituent atoms irrespective of its degree of hydrogenation. Then come the cyclopentamethylenearsines as six-membered ring compounds, followed by their derivatives (tetrahydroarsinolines, arsacridines, etc.) which contain the same ring. Next come the smallest ring systems which contain carbon, arsenic, and one other element. All the five-membered ring systems are dealt with, in order of increasing atomic weight of the third element. Hence the carbon–arsenic–nitrogen ring systems come first, then the carbon–arsenic–oxygen systems, etc. The six-membered ring systems are then dealt with similarly: for this purpose and for orderly classification a second arsenic atom in the ring has been counted as a third element.

The nomenclature of the cyclic compounds is often simple, but certain difficult problems arise. If we again take the arsenic compounds as examples, the names of the simpler noncyclic derivatives give no trouble. The main types may be exemplified as follows:

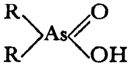
$C_6H_5AsCl_2$	Phenyldichloroarsine
$(C_6H_5)_2AsCl$	Diphenylmonochloroarsine
$(C_6H_5)_3As$	Triphenylarsine
$(C_6H_5)_3AsCl_2$	Triphenylarsine dichloride
$(C_6H_5)_3AsO(S)$	Triphenylarsine oxide (or sulfide)
C_6H_5AsO	Phenylarsenoxide
$C_6H_5AsO(OH)_2$	Phenylarsonic acid
$(C_6H_5)_2AsO(OH)$	Diphenylarsinic acid

The names of the compounds used in synthesizing the cyclic compounds and of many of the cyclic compounds themselves usually follow very simply from those of the above main types.

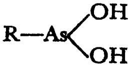
It should be noted, however, that a recent change in the British nomenclature of the acids derived from the Group V elements has created an unfortunate discrepancy between the American nomenclature (as used in *Chemical Abstracts*) and the British nomenclature (as used in *British Abstracts*). This is shown in the following table, in which the American name [*cf. Chemical Abstracts*, **39**, 5939 (1945)] is given immediately below each compound, and the British name in parenthesis beneath; in these formulas the symbol R represents an alkyl, aryl, or halogen group.



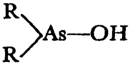
Arsonic acid
(Arsonic acid)



Arsinic acid
(Arsonous acid)



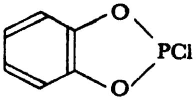
Arsonous acid
(Arsinic acid)



Arsinous acid
(Arsinous acid)

The analogous phosphorus and antimony acids are similarly named; thus, in place of an arsonic acid, one has a phosphonic or stibonic acid, and in place of an arsinous acid one has a phosphinous or stibinous acid.

The American nomenclature has been adopted throughout this book. In the author's opinion it is more logical than the British system, inasmuch as it ensures that the names of the two types of organic acid in which the Group V element has its higher valency have the suffix *ic*, and their salts the suffix *ate*, and those of the two types in which the element has its lower valency have the suffix *ous*, and their salts the suffix *ite*: the names thus fall in line with the long-established names of the purely inorganic acids, for example, phosphoric acid, $OP(OH)_3$, and the phosphates, and phosphorous acid, $P(OH)_3$, and the phosphites. It should be noted, however, that this discrepancy must introduce different names for certain compounds according to the system of nomenclature used. For example, the compound (I) is regarded in the American system as being an ester of pyrocatechol and chlorophosphonous acid and hence is termed *o*-phenylenechlorophosphonite; in the British system this becomes *o*-phenylene-chlorophosphinate.

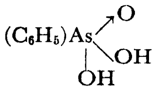


(I)

Another difficulty occasionally arises in the name to be applied to the parent compound of a given heterocyclic system, of which all members will be regarded as derivatives. Some of the names used in the past, such as *o,o′*-diphenylylenearsines and xenylene-2,2′-stibines are too unsatisfactory to be perpetuated. In seeking more suitable names, an attempt has been made to maintain a reasonable balance between a strictly logical system on the one hand and practical convenience on the other. For example, the term "arsa-carbazole" has been applied in the past to compounds in which the nitrogen atom of carbazole could be regarded as having been replaced by arsenic, but logically this term means carbazole in which one ═CH— group has been replaced by the ═As— group. It is hoped that the term 9-arsafluorene, although possibly strange to many chemists, will not be unacceptable to them. Here, the prefixed number 9 makes it clear that the term *arsa* implies that the —CH_2— group has been replaced by the —AsH— group. In certain cases I have retained a well-established term because it has the merit of great convenience, even if logically, or systematically, it is inaccurate. For example, the term *arsacridine* is used in place of the more logical *10-arsa-anthracene* (p. 49), partly because it has become reasonably well established and partly because it allows a convenient term such as *arsacridinic acid* to be applied to the corresponding cyclic arsinic acid, for which the 10-arsa-anthracene nomenclature gives no such simple name. It is clear, however, that it would be of immense help if the chemists of the English-speaking nations would come to unanimous agreement concerning the nomenclature of these heterocyclic systems before confusion in this rapidly expanding field becomes greater.

With regard to the numbering of the heterocyclic systems, that adopted in *Chemical Abstracts* has been adhered to in most cases as representing standard American practice. In certain cases, however, this numbering differs strikingly for strictly analogous types of compounds—a fact that becomes more obvious in a monograph of this type than in the vast indexes of *Chemical Abstracts*—and moreover is often at variance with that advocated in the *Ring Index*. When the numbering ultimately adopted here differs from that in *Chemical Abstracts*, the two systems have been indicated clearly, so that transference from one to the other (if desired) is quite simple.

One point concerning the use of symbols requires brief discussion. In a compound such as trimethylamine oxide the electronic content of the nitrogen atom demands a coordinate link between the nitrogen and the oxygen, and the formula is written $(CH_3)_3N \rightarrow O$ or $(CH_3)_3\overset{+}{N}-\overset{-}{O}$. The oxides and sulfides of the tertiary phosphines, arsines, and stibines have until recently been depicted similarly, for example, $(C_6H_5)_3P \rightarrow O$, $(C_6H_5)_3As \rightarrow S$, and phosphonic and arsonic acids have also been depicted as having coordinate links, as



$$(C_6H_5)As(\rightarrow O)(OH)(OH)$$

Recent measurements of the interatomic distances between phosphorus and oxygen atoms in phosphorus oxychloride, Cl_3PO, and other analogous compounds show, however, that this distance is too small to be linked by one covalent bond, and that, therefore, the link probably has some double bond character. The exact nature of the bond in these compounds remains uncertain at present, but it is probably a resonance hybrid between a coordinate link and a double bond, with the proportion of double bond character increasing from phosphorus through to antimony. Chemists have no symbol for such a hybrid bond, and for such compounds, therefore, a double bond has been used throughout (for printing convenience). It will be understood that in all such cases this symbol refers to this ill-defined hybrid bond and not to the classical double bond. In the few compounds mentioned in which arsenic is coordinated to a heavy metal such as palladium, however, the coordinate link symbol has been retained because in such compounds there is at present no evidence against the existence of this link.

A glance through this book will show that the heterocyclic derivatives of arsenic are considerably greater—both in variety of types and in actual numbers of compounds—than those of phosphorus, antimony, or bismuth. Of course, this statement is true of organic derivatives of these elements in general, whether cyclic or otherwise. It is not difficult to find the reasons for this predominance of the arsenic compounds. First, there has been for many years an insistent demand for organic arsenic compounds, arising originally from their application as drugs and later (from the days of

World War I), from their potential value as offensive agents in warfare. Second, the synthesis of organic arsenic compounds is facilitated immensely by certain valuable reactions which have only a limited application—or often no application at all—in the synthesis of analogous phosphorus, antimony, and bismuth derivatives.

Two reactions stand out prominently in this respect. In the aliphatic field, the reaction initiated by Meyer in Germany and widely developed by Dehn in America must be noted. If, for example, arsenic trichloride and methyl iodide are added to aqueous sodium hydroxide and the solution is boiled, sodium methyl arsonate results:

$$AsCl_3 + CH_3I + NaOH \longrightarrow CH_3AsO(ONa)_2$$

If the sodium salt is now added to concentrated hydrochloric acid containing a trace of potassium iodide and sulfur dioxide is passed through the mixture, reduction to methyldichloroarsine, CH_3AsCl_2, occurs readily. The Meyer reaction may now be repeated with this dichloroarsine, which when similarly boiled with methyl iodide and aqueous sodium hydroxide gives the sodium salt of dimethylarsinic acid:

$$CH_3AsCl_2 + CH_3I + NaOH \longrightarrow (CH_3)_2AsO(ONa)$$

The latter can be reduced in turn, under the previous conditions, to dimethylmonochloroarsine, $(CH_3)_2AsCl$, and this compound can be subjected to a final Meyer reaction to give trimethylarsine oxide:

$$(CH_3)_2AsCl + CH_3I + NaOH \longrightarrow (CH_3)_3AsO$$

Tertiary arsine oxides usually undergo very ready reduction (usually in chloroform solution) by sulfur dioxide in the presence of a trace of potassium iodide, even at room temperature, to give the tertiary arsine. The Meyer reaction is thus particularly valuable for the preparation of arsines containing different alkyl groups. This reaction, it should be emphasized, cannot be applied to the analogous phosphorus compounds, and in any case there is no ready method by which the exceedingly stable tertiary phosphine oxides can be reduced to the tertiary phosphines themslves. Furthermore, the Meyer reaction cannot be applied satisfactorily to the synthesis of antimony compounds.

In the aromatic field, the Bart reaction is of great value for the synthesis of arsonic acids and the many derivatives that can be prepared from them. In this reaction an aromatic amine is diazotized and the solution made alkaline and then treated with sodium arsenite. Nitrogen is evolved, with the formation of the corresponding arsonic acid as the sodium salt. Aniline, for example, will thus furnish the sodium salt of phenylarsonic acid:

$$C_6H_5N_2ONa + NaAsO_2 \longrightarrow C_6H_5AsO(ONa)_2 + N_2$$

If phenyl arsenoxide, C_6H_5AsO, is used in place of the sodium arsenite, the sodium salt of the corresponding diaryl arsinic acid is obtained:

$$C_6H_5N_2ONa + C_6H_5AsO \longrightarrow (C_6H_5)_2AsO(ONa) + N_2$$

Since the arsonic acid can be reduced readily to the dichloroarsine, $C_6H_5AsCl_2$, for example, and the arsinic acid to the monochloroarsine, $(C_6H_5)_2AsCl$, by the reduction outlined above, the wide value and scope of this reduction will be obvious. The Bart (or Bart-Schmidt) reaction can be applied similarly to the preparation of the corresponding stibonic and stibinic acids, but the yields are usually much lower. It cannot be applied to the preparation of the corresponding phosphorus derivatives.

Many examples of the Meyer and Bart reactions occur in this book, and the vast role they have played in the development of the chemistry of organic derivatives of arsenic must be obvious.

To the practical chemist at the bench the organic derivatives of arsenic must always be very attractive because many separate so readily in such beautifully crystalline condition. After a long and often wearisome synthesis, this factor satisfies not only the chemist's esthetic appreciation of beauty, but also his sense of ultimate justice! Unfortunately this property of ready and decisive crystallization is much rarer in the organic derivatives of phosphorus, antimony, and bismuth.

These heterocyclic derivatives of the Group VB elements also make a strong appeal to the stereochemist, for they have provided solutions for several problems that might never have been solved by the use of noncyclic derivatives alone.

A cursory glance through this monograph will indicate how little is known of the heterocyclic derivatives of phosphorus, arsenic, antimony, and bismuth compared with our vast knowledge of the similar derivatives of nitrogen. However, this glance should also indicate to the reader the wide and fruitful field of investigation that the heterocyclic derivatives of these four elements still offer to the chemist.

A short account of heterocyclic derivatives of silicon has been included because in some respects (particularly their synthesis) they bear a strong resemblance to the corresponding derivatives of the Group VB elements.

This monograph was started while I held a visiting Senior Professorship at the University of Hawaii, and completed on my return to Cambridge. I would like to take this opportunity to thank the authorities of the University of Hawaii most sincerely for the many facilities they so generously placed at my disposal.

Comments and criticisms concerning the contents of this book would be warmly welcomed by the author.

F. G. MANN

January, 1950
Cambridge, England

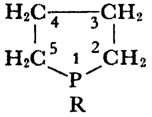
CHAPTER 1

Heterocyclic Derivatives of Phosphorus

Five-Membered Ring Systems Containing Only Carbon and Phosphorus

Cyclotetramethylenephosphines

These have the general formula (I), R.I. 113*, and the ring is numbered as shown. The phenyl compound (R = Ph) has been prepared[1] by the interaction of phenyldichlorophosphine and the Grignard reagent prepared from tetramethylene dibromide, *i.e.*, $(\cdot CH_2CH_2MgBr)_2$ in ether. This compound should therefore be called 1-phenyl- (or *P*-phenyl-)-cyclotetramethylenephosphine. It is a colorless oil, b.p. 132–133°/17 mm., having a very strong characteristic "phosphine" odor; it is only slowly oxidized by air.



(I)

It shows the normal chemical properties of a tertiary phosphine. Thus it gives a mercuric chloride addition product, of composition $C_{10}H_{13}P \cdot HgCl_2$, colorless crystals, m.p. 143–144° (decomp.), and it also gives the following quaternary phosphonium salts: methiodide, an oil which has not been obtained in crystalline form; ethiodide, colorless crystals, m.p. 122°; *n*-propyl iodide, colorless crystals, m.p. 153–154°.

---

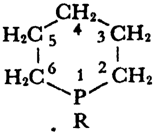
[1] Grüttner and Krause, *Ber.*, **49**, 438 (1916).

* Patterson and Capell, *The Ring Index*, Reinhold, New York, 1940, p. 44. Subsequent references to *The Ring Index* will be characterized only by the Ring Index number. These numbers follow a natural sequence.

Six-Membered Ring Systems Containing Only Carbon and Phosphorus

Cyclopentamethylenephosphines

These compounds have the general formula (II), R.I. 204, and are closely similar in preparation and properties to their tetramethylene homologs already described. The 1-phenylcyclopentamethylenephosphine (II, R = Ph) has been prepared by the action of phenyldichlorophosphine on the di-Grignard reagent prepared from pentamethylene dibromide, *i.e.*, $CH_2(CH_2CH_2MgBr)_2$. It is a colorless oil, b.p. 143–144°/16–18 mm., 154–155°/22–24 mm., having the characteristic "phosphine" odor, and not markedly oxidized by air. It gives a mercuric chloride addition product, $C_{11}H_{15}P \cdot HgCl_2$, colorless crystals, m.p. 172° (decomp.), and a quaternary ethiodide, also colorless crystals, m.p. 188°.

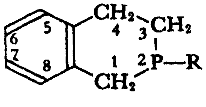


(II)

The 1-*p*-tolyl homolog[2] (II, R = *p*-tolyl), similarly prepared using *p*-tolyldichlorophosphine, is a colorless liquid, b.p. 167–168°/26 mm., giving a mercuric chloride addition product, $C_{12}H_{17}P \cdot HgCl_2$, m.p. 157°, and a quaternary ethiodide, m.p. 163–164°.

1,2,3,4-Tetrahydroisophosphinolines

These compounds have the general formula (III), and can therefore be regarded as the phosphorus analogs of tetrahydroisoquinoline. The

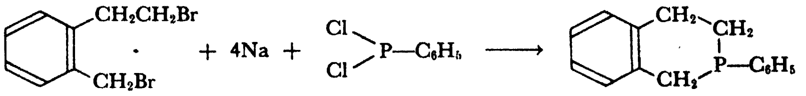


(III)

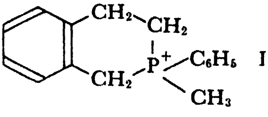
---

[2] Grüttner and Wiernik, *Ber.*, **48**, 1473 (1915).

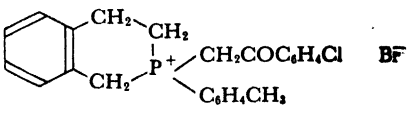
2-phenyl derivative (III, R = C_6H_5) was first prepared by Holliman and Mann[3] by the interaction of *o*-2-bromoethylbenzyl bromide, phenyldichlorophosphine, and sodium in boiling ether:



The yield of the oily phosphine was so low, however, that it was converted to the crystalline methiodide, *i.e.*, 2-methyl-2-phenyl-1,2,3,4-tetrahydroisophosphinolinium iodide (IV), m.p. 116–118°. The use of *p*-tolyldichlorophosphine in this reaction similarly gave the 2-*p*-tolyl derivative[4] (III, R = *p*-tolyl), but again the yield was so low that the phosphine was characterized by combination with *p*-chlorophenacyl bromide to give the crystalline 2-*p*-chlorophenacyl-2-*p*-tolyl-1,2,3,4-tetrahydroisophosphinolinium bromide (V), m. p. 227–230°.



(IV)



(V)

The low yields in the above condensation were attributed by these authors to the fact that as soon as the cyclic tertiary phosphine was formed it undoubtedly combined with unchanged bromide to give a quaternary salt.

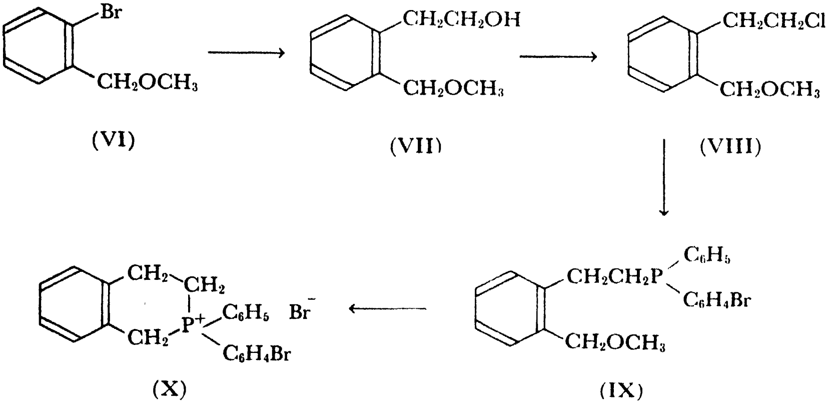
To overcome this difficulty, a second synthesis[4] was successfully developed. For this purpose, *o*-bromobenzyl methyl ether (VI) was converted into a Grignard reagent, which was then caused to react with ethylene oxide to give *o*-2-hydroxyethylbenzyl methyl ether (VII). This was then converted by thionyl chloride to the 2-chloroethyl derivative (VIII), which was again converted into a Grignard reagent, and the latter, when treated with *p*-bromophenyl-phenyl-monochlorophosphine, readily gave *p*-bromophenyl-phenyl-2-(*o*-methoxymethylphenyl)ethyl phosphine (IX).

---

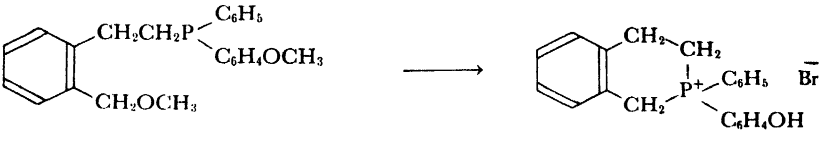
[3] Holliman and Mann, *J. Chem. Soc.*, **1943**, 547.

[4] Holliman and Mann, *J. Chem. Soc.*, **1947**, 1634.

When this compound was heated with hydrogen bromide in glacial acetic acid solution, the methoxymethyl group was converted to the bromomethyl group, and the latter then cyclized to give 2-*p*-bromophenyl-2-phenyl-1,2,3,4-tetrahydroisophosphinolinium bromide (X), colorless crystals which melted at 137–149° to a viscous cloudy liquid which resolidified and melted at 218–221°. This phosphonium bromide was also characterized by conversion to the phosphonium picrate, yellow crystals, m.p. 186–187°. The two different aryl groups were introduced into the phosphorus compound (X) to obtain a quaternary phosphonium salt which would contain an asymmetric phosphorus atom and thus be capable of resolution into optically active forms. The bromide (X) was therefore converted to the corresponding isophosphinolinium *d*-camphor sulfonate, but recrystallization of this salt gave no evidence of resolution. No crystalline salts with other optically active acids could be obtained.



Repetition of the synthesis using *p*-anisyl-phenyl-monochlorophosphine, however, gave *p*-anisyl-phenyl-2-(*o*-methoxymethylphenyl)ethyl phosphine (XI) and when this compound was heated similarly with hydrogen bromide, cyclization occurred as before, but simultaneously the *p*-anisyl group was demethylated: consequently the final product was 2-*p*-hydroxyphenyl-2-phenyl-1,2,3,4-tetrahydroisophosphinolinium bromide (XII). This salt was converted to the corresponding *d*-camphor sulfonate, which on recrystallization furnished the optically pure *d*-phosphinolinium *d*-camphor sulfonate, m.p. 174–175°, $[M]_D + 113.5°$ in ethanolic solution. This salt in turn furnished the optically pure *d*-bromide (XII), having $[M]_D + 32.9°$ in ethanolic solution. This is the only quaternary phosphonium salt that has been obtained in optically active form.



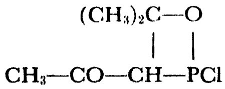
(XI) (XII)

It should be noted that compounds in the isomeric 1,2,3,4-tetrahydrophosphinoline series, which would form the phosphorus analogs of tetrahydroquinoline, are at present unknown. In the corresponding arsenic compounds, however, members of both the isomeric series are known (see Section II).

Four-Membered Ring Systems Containing Carbon, Phosphorus, and Oxygen

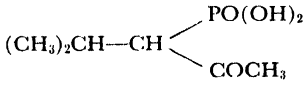
Michaelis[5] has shown that acetone condenses with phosphorus trichloride in the presence of aluminum chloride to give a colorless product of composition $C_6H_{10}O_2ClP$, having b.p. 154°/100 mm. and m.p. 35–36°: the yield of this compound is 10% calculated on the phosphorus trichloride taken.

Michaelis[5] has allotted formula (I), R.I. 32, to this compound. It certainly contains 3-covalent phosphorus, because in petrol solution in



$$\begin{array}{l} \qquad\quad (CH_3)_2C\text{—}O \\ \qquad\qquad\quad |\quad\ \ | \\ CH_3\text{—}CO\text{—}CH\text{—}PCl \end{array}$$

(I)



(II)

the cold it adds on a molecular equivalent of bromine to form the compound $C_6H_{10}O_2ClBr_2P$, colorless crystals, m.p. 142°, which react with water to give mesityl oxide, hydrochloric acid, hydrobromic acid, and phosphoric acid. The compound (I) similarly adds on chlorine to give a product of composition $C_6H_{10}O_2Cl_3P$, colorless crystals, m.p. 115°: it is stated that, when this product is treated with aqueous silver nitrate solution, two-thirds of the chlorine are immediately precipitated, and the remainder only slowly on boiling.

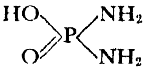
---

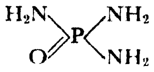
[5] Michaelis, *Ber.*, **17**, 1273 (1884); **18**, 898 (1885).

The precise structure of the compound (I) remains uncertain without further evidence. Michaelis states that it reacts with water, slowly in the cold, more rapidly when hot, to give "isopropylacetonylphosphinic acid," to which structure (II) is allotted. This acid has m.p. 63°, crystallizes with one molecule of water, and is described as a strong dibasic acid giving salts which are usually well characterized: it gives a crystalline anhydrous oxime and has evidently retained one carbonyl group. It should be noted, however, that it is unlikely that an acid of structure (II) would be produced by the hydrolysis of a compound of structure (I), and these compounds clearly invite further investigation.

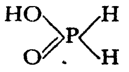
Five-Membered Ring Systems Containing Carbon, Phosphorus, and Nitrogen

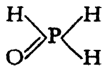
A number of compounds are known which could be regarded systematically as cyclic substitution products of the diamide (I) and the triamide (II) of phosphoric acid, and of the corresponding thio derivatives: for the present purpose, the more modern nomenclature is employed and they are therefore considered as substitution derivatives of


(I)


(II)

phosphinic acid (III) and of phosphine oxide (IV) (*cf.* page 2). Thus, Autenrieth and Bölli[6] have shown that when phenyldichlorophosphinate

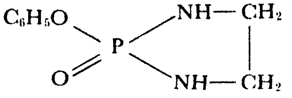

(III)


(IV)

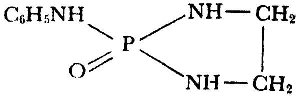
---

[6] Autenrieth and Bölli, *Ber.*, **58**, 2144 (1925).

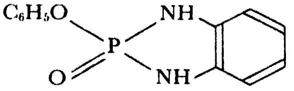
$C_6H_5O.POCl_2$, is mixed with an excess of dilute ethylenediamine at 0°, the compound phenyl ethylenediamino-phosphinate (V), R.I. 69, is obtained as a colorless microcrystalline powder, m.p. 196°, which is quite insoluble in water and the usual organic liquids. The *p*-tolyl homolog has m.p. 204° and similar properties. When anilinodichlorophosphine oxide, $C_6H_5NH.POCl_2$, is similarly treated with ethylenediamine, the compound anilinoethylenediaminophosphine oxide (VI) is obtained, m.p. 232°, and is also insoluble in all the normal solvents. These properties prevent the determination of the molecular weight of these compounds. For this reason, more convincing results were obtained by treating the dichlorophosphinate with *o*-phenylenediamine, whereby on heating at 170° or (better) by refluxing in benzene solution, phenyl *o*-phenylenediaminophosphinate (VII), R.I. 690, is formed as colorless needles which can be recrystallized from ethanol or hot water, and then have m.p. 185°. Molecular weight determinations agree with formula (VII). This compound is soluble in several organic liquids: it is also surprisingly stable, as it is unaffected by hot water or even hot dilute hydrochloric acid, although alkalis decompose it. The *p*-tolyl analog has similar properties and melts at 158°. If anilinodichlorophosphine oxide is treated with *o*-phenylenediamine in boiling benzene, the corresponding anilino-*o*-phenylenediaminophosphine oxide (VIII) is obtained, colorless crystals from aqueous ethanol, m.p. 214°: these are also soluble in a number of solvents.



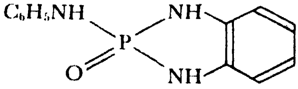
(V)



(VI)



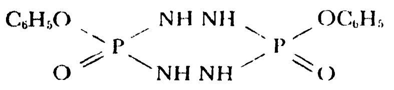
(VII)



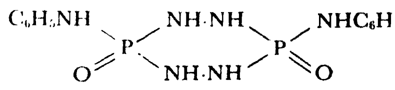
(VIII)

There is thus a striking contrast between the insolubility of the ethylene compounds (V) and (VI), and the reasonably ready solubility of the *o*-phenylene analogs (VII) and (VIII). It is reminiscent of the insolubility of oxamide and the much greater solubility of, for example, phthalamide and succinamide, and it may imply that compounds (V) and (VI) are highly and stably associated, and thus do not have the simple structures depicted in these formulas.

It is convenient to mention here the similar reaction which occurs when hydrazine is used, although a six-membered carbon-free ring is thus obtained. When phenyldichlorophosphinate is added to an ice-cold agitated aqueous solution of hydrazine hydrate, the compound (IX), R.I. 220, *i.e.*, diphenyl-bis-1,2-hydrazinodiphosphinate, is formed: it separates as colorless crystals from hot water or ethanol, m.p. 132°. Its structure is confirmed by molecular weight determinations. The *p*-tolyl analog, m.p. 168°, has similar properties. Anilinodichlorophosphine oxide reacts with hydrazine hydrate to form the parallel compound (X), *i.e.*, bis-1,2-hydrazino-bis(anilinophosphine oxide), colorless crystals, m.p. 208–210°, which are slightly soluble in cold water but readily soluble in ethanol.

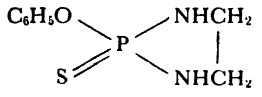


(IX)

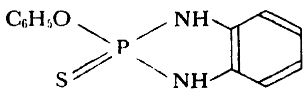


(X)

The use of phenyldichlorothiophosphinate,[7] $C_6H_5O.PSCl_2$, in the above reactions gives the corresponding thio derivatives, which have properties closely similar to those of the oxygen analogs. Thus the dichlorothiophosphinate reacts with dilute aqueous ethylenediamine to give phenylethylenediaminothiophosphinate (XI), white micro-



(XI)



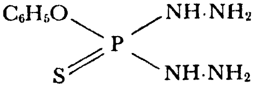
(XII)

---

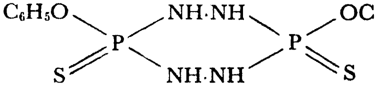
[7] Autenrieth and Meyer, *Ber.*, **58**, 848 (1925).

crystalline powder, m.p. 189°, insoluble in all the usual solvents. *o*-Phenylenediamine gives phenyl *o*-phenylenediaminothiophosphonite (XII), white crystals, m.p. 185°: both this compound and its *p*-tolyl homolog, m.p. 147°, are soluble in various solvents, can be recrystallized from hot water or ethanol, and are unaffected by hot dilute hydrochloric acid.

It is noteworthy that the dichlorothiophosphinate reacts with aqueous hydrazine to give—according to the conditions—either phenyldihydrazinothiophosphinate (XIII), colorless leaflets from ethanol, m.p. 85°, or diphenyl-bis-1,2-hydrazinodithiophosphinate (XIV), colorless prisms from ethanol, m.p. 183°. The former condenses with benzaldehyde to give a dibenzylidene derivative, $C_6H_5OPS(NHN{:}CHC_6H_5)_2$, m.p. 115°, but the compound (XIV) does not, of course, from a benzylidene derivative.



(XIII)



(XIV)

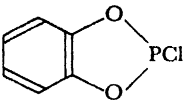
Five-Membered Ring System Containing Carbon, Phosphorus, and Oxygen

o-Phenylenechlorophosphonites

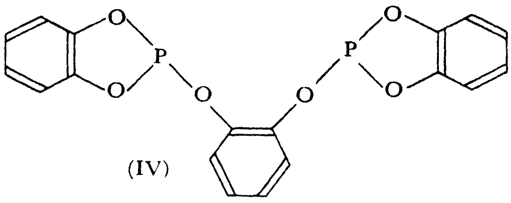
A number of compounds have been recorded which can systematically be regarded as esters of pyrocatechol and phosphorous acid, in which in some examples one hydroxyl group of the acid has been replaced by chlorine. They are usually stable when dry, but even with cold water undergo rapid hydrolysis to their original components. Thus, Knauer[8] has shown that pyrocatechol and phosphorus trichloride when boiled together for twelve hours form a crude product which on fractional distillation gives first *o*-phenylenechlorophosphonite (III), b.p. 140°/65 mm., solidifying to a white mass, m.p. 30°, and second a viscous yellow oil, b.p. > 360°/65 mm., the composition of which corresponds to tri-*o*-phenylene diphosphite (IV). The chlorophosphonite (III), R.I. 717, when treated with water, hydrolyzes with considerable evolution of heat and with the formation of pyrocatechol, phosphorous acid, and hydrogen chloride. The compound (IV) can also be prepared by heating the chlorophosphonite with one more equivalent of pyrocatechol.

---

[8] Knauer, *Ber.*, **27**, 2569 (1894).

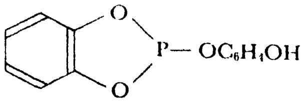


(III)



(IV)

The interaction of pyrocatechol and phosphorus trichloride has been reinvestigated by Anschutz and Broeker,[9] who have confirmed the formation of the chlorophosphonite (III), b.p. 80°/10 mm., and the diphosphite (IV), b.p. 242–243°/14 mm., but have shown that *o*-hydroxyphenyl-*o*-phenylene phosphite (V) is formed as an intermediate compound, b.p. 155°/12 mm., m.p. 112–113°. When the reaction is carried out in benzene, these three compounds can be isolated by fractional distillation of the product. These authors also show that the hydroxyphenylphosphite (V), when heated with the chloro-phosphonite (III) at 120°,



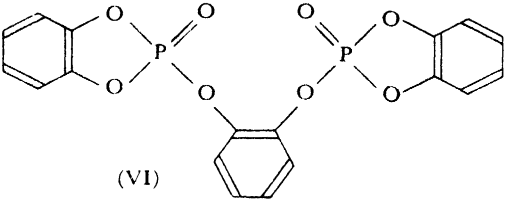
(V)

gives the diphosphite (IV), and that the latter compound, when heated with phosphorus trichloride in a sealed tube at 160°, gives the chlorophosphonite (III).

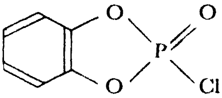
It is noteworthy that when pyrocatechol is heated with phosphorus oxychloride,[8] the oxide of the compound (IV), *i.e.*, tri-*o*-phenylene diphosphate (VI), is formed as a very viscous syrup, and this compound, when heated in turn with an excess of phosphorus oxychloride, forms *o*-phenylenechlorophosphonate (VII), a colorless liquid, b.p. 162°/55 mm., which forms a crystalline mass, m.p. 35°. This indirect method for the preparation of the chlorophosphonate (VII) is in marked contrast to that of *o*-phenylenechloromonothiophosphonate (VIII),[9] which can readily be prepared by the action of sulfur on the chlorophosphinate (III) at 195°.

---

[9] **Anschutz and Broeker, *Ber.*, 61, 1264 (1928).**

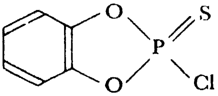


(VI)

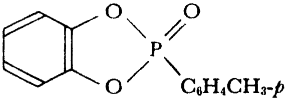


(VII)

Michaelis[10] has shown that pyrocatechol reacts with *p*-tolyldichlorophosphine oxide, $CH_3.C_6H_4.POCl_2$, to give the *o*-phenylene ester (IX) of *p*-tolylphosphonic acid, colorless crystals, m.p. 81°, b. p. > 360°, which reacts with water to give pyrocatechol and *p*-tolylphosphonic acid.



(VIII)



(IX)

Many compounds[11] similar to the chlorophosphonite (III), but with the chloro group replaced by aryloxy, alkoxy, and aryl groups, have been prepared.

Six-Membered Ring Systems Containing Carbon, Phosphorus, and Nitrogen

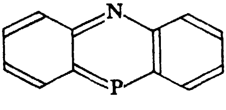
Phenphosphazines

These compounds are regarded as derivatives of the unknown phenphosphazine (I); however, since all the few known derivatives are of type (II), they are known as 10-R-5,10-dihydrophenphosphazines. The numbering in (II) brings these compounds into line with the phenarsazines (see page 80), the phenoxarsines (page 100), the arsanthrenes (page 117) and the phenoxstibines (page 152), and is that employed in the *Ring Index* (No. 1855). It should be noted, however, that the numbering shown in (III) is that employed in *Chemical Abstracts*.

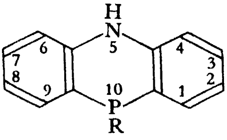
---

[10] Michaelis, *Ann.*, **293**, 265 (1896).
[11] Anschutz, Walbrecht and Broeker, *J. prakt. Chem.*, **133**, 65 (1932)

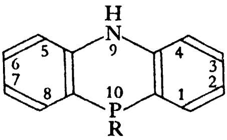
Michaelis and Schenk[11a] stated that diphenylamine and phosphorus trichloride had no interaction in the cold, but when heated with zinc chloride in a sealed tube at 250 ° gave a marked evolution of hydrogen chloride and a viscous oil. The latter, when treated with water, gave a white powdery substance of composition $C_{12}H_{10}ONP$, which they suggested might be 10-hydroxy-5,10-dihydrophenphosphazine (II, R = OH). The compound possessed considerable stability because it could be nitrated without loss of phosphorus.



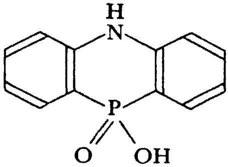
(I)



(II)



(III)



(IV)

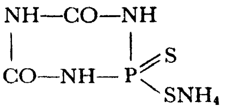
The formation of this cyclic system has been reinvestigated recently by Sergeev and Kudryashov,[11b] who state that when diphenylamine and phosphorus trichloride are heated at 200 ° for six hours, and the product extracted with water, the above 10-hydroxy derivative (II, R = OH) is obtained: it shrinks (without melting) at 215–216 °. When it was treated with thionyl chloride, it gave the 10-chloro compound as a heavy oil which was not purified, but which when treated with sodium ethoxide in ethyl alcohol solution gave 10-ethoxy-5,10-dihydrophenphosphazine (II, R = OEt), m.p. 151.5–152°.

[11a] Michaelis and Schenk, *Ann.*, **260** ,1 (1890).

[11b] Sergeev and Kudryashov, *J. Gen. Chem.* (*U. S. S. R.*), **8**, 266 (1938).

When the 10-hydroxy compound was boiled in tetralin solution, it underwent atmospheric oxidation and yielded phenphosphazinic acid (IV), which did not melt below 250°. This acid gave a silver salt, a methyl ester (m.p. 112–114°) and an ethyl ester (m.p. 99°): a nitro derivative was also described.

Hemmelmayr[12] has stated that when a mixture of urea and phosphorus pentasulfide is heated at 100° and the product then extracted with cold water, colorless crystals can ultimately be isolated, which on heating decompose at 252°, and whose composition agrees with a formula,



$C_2H_7O_2N_4S_2P$. Hemmelmayr considers this compound to be an ammonium salt having the cyclic structure shown (R.I. 132). Since, however, very little evidence for this structure is given, acceptance of this heterocyclic system must await further information.

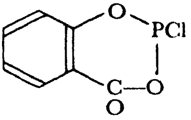
Six-Membered Ring Systems Containing Carbon, Phosphorus, and Oxygen

Salicylchlorophosphonite

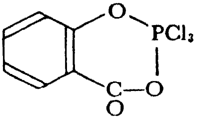
This compound is similar in type to the above esters of pyrocatechol and phosphorous acid: it differs in that in the salicyl compound one hydroxyl group of the phosphorous acid can be regarded as having acted as an acidic group in order to esterify the phenol group of salicylic acid, and another hydroxyl group of the phosphorous acid has behaved as such in order to esterify the carboxylic acid group of the salicylic acid. Thus, Anschutz and Emery[13] have shown that salicylic acid reacts with phosphorus trichloride to give salicylchlorophosphonite (I), a colorless liquid, b.p. 127°/11 mm., which, when treated with water, readily hydrolyzes to salicylic acid and phosphorous acid. If phosphorus pentachloride is used in the above preparation, salicyltrichlorophosphonate (II) is formed as a liquid, b.p. 167°/11 mm.

---

[12] Hemmelmayr, *Monatsh.*, **26**, 772 (1905).
[13] Anschutz and Emery, *Ann.*, **239**, 304, 314 (1887).



(I)



(II)

Ten-Membered Ring Systems Containing Carbon, Phosphorus, and Oxygen

It has been stated by Carré[14] that, if phosphorus trichloride is added to a solution of ethylene glycol in anhydrous ether, a reaction occurs with the formation of two products, the major product being soluble in the ether and the minor product insoluble. When the ether is evaporated from the solution of the major product, the liquid residue cannot be distilled without decomposition—even in a vacuum. Carré claims, however, that analysis of the crude residue indicates that this product has the composition corresponding to the structure (I), R.I. 309, and that this is confirmed by its molecular weight in freezing benzene (experimental value, 244; theoretical value, 253).

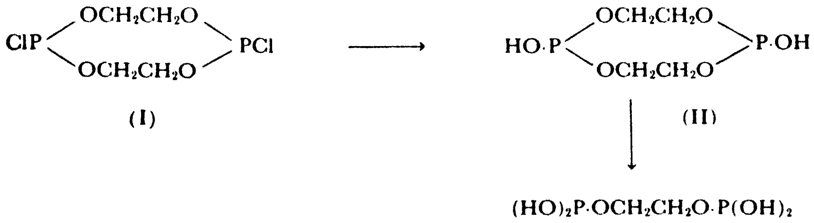
Carré states that when the compound (I) is hydrolyzed with water using external cooling, and the solution subsequently treated with calcium carbonate, two calcium salts can be isolated, analysis indicating that one has the composition $P_2(OCH_2CH_2O)_2O_2Ca$ and the other the composition $P_2(OCH_2CH_2O)(OH)_2O_2Ca$. Consequently, he argues that the dichloro compound (I) undergoes hydrolysis initially to give the corresponding dihydroxy compound (II), and that this compound is very unstable and rapidly undergoes further hydrolysis with liberation of a molecule of ethylene glycol and the formation of the noncyclic derivative (III).

The minor product which is formed in the initial reaction and is insoluble in ether has been identified as $ClP(OH)(OCH_2CH_2Cl)$ by

---

[14] Carré, *Compt. rend.*, **136**, 757 (1903).

Carré. He adds that, if phosphorus trichloride is added to ethylene glycol without ether as a solvent, the compound $Cl_2P(OCH_2CH_2Cl)$ is formed. This can be distilled in a vacuum, but no boiling point is quoted.



(I) (II) (III)

The interaction of phosphorus trichloride and ethylene glycol has been investigated more recently by Rossiiskaya and Kabachnik,[14a] and also by Saunders *et al.*[14b] The latter workers, using dioxane as a solvent, have obtained considerable evidence that the ten-membered ring compound (II) is the major product formed under the conditions they employ.

[14a] Rossiiskaya and Kabachnik, *Bull. Acad. Sci. Russia*, **1947**, 509.

[14b] Cook, Ilett, Saunders, Stacey, Watson, Wilding, and Woodcock, *J. Chem. Soc.*, **1949**, 2921.

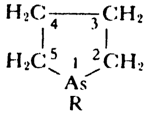
CHAPTER II

The Heterocyclic Derivatives of Arsenic

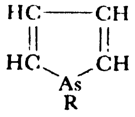
Five-Membered Ring Systems Containing Only Carbon and Arsenic

Cyclotetramethylenearsines

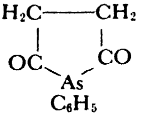
These compounds have the general formula (I), R.I. 107, where R can be an alkyl, aryl, or halogen group, and the constituent atoms of the ring are numbered as shown. It will be obvious that the compound in which R = H, if it were known, would be the arsenic analog of pyrolidine, and it has therefore been termed arsenolidine. The true arsenic analog of pyrrole, the arsenoles, of general formula (II), are also unknown, but their mono- and di-benzo derivatives, the arsindoles and arsafluorenes, respectively, are known (pp. 26 and 36).



(I)



(II)



(III)

Grüttner and Krause[15] have shown that phenyldichloroarsine reacts with the di-Grignard reagent obtained from tetramethylene dibromide, *i.e.*, with $(\cdot CH_2\cdot CH_2MgBr)_2$, in cold ether to give 1-phenyl-(or As-phenyl)-cyclotetramethylenearsine (I, R = C_6H_5), which is obtained as a colorless liquid, b.p. 128.5°/15–16 mm., having a faint odor. The arsine is not readily oxidized in air. It has the normal properties of a tertiary arsine; for example, it combines with chlorine to form a colorless crystalline dichloride, $C_{10}H_{13}AsCl_2$, m.p. 120.5°, and with mercuric chloride to form a mercuri-chloride, $C_{10}H_{13}As\cdot HgCl_2$, m.p. 160–162°. It also forms the

[15] Grüttner and Krause, *Ber.*, **49**, 441 (1916).

following quaternary arsonium salts, all of which are colorless crystalline compounds: methiodide, m.p. 135–136°; ethoidide, m.p. 85–86°; *n*-propyl iodide, 123–124°; isopropyl iodide, m.p. 113–114°.

It has been stated by Das-Gupta[16] that succinyl chloride $(\cdot CH_2COCl)_2$, phenyldichloroarsine, and sodium react together in benzene containing some ethyl acetate to give "succinylphenylarsine" or 1-phenyl-2,5-diketocyclotetramethylenearsine (III), a colorless liquid having b.p. 119–120°/10 mm. This compound gives the quaternary salts: methiodide, m.p. 176°; ethiodide, 165–167°. It is also stated to give a picrate, m.p. 117° (although tertiary arsines do not usually give picrates), and a mercurichloride, m.p. 245°. When reduced with sodium in an ethanol–toluene solution, it gives the above 1-phenylcyclotetramethylenearsine, b.p. 125–130°/15 mm.

Steinkopf, Schubert, and Roch[17] have similarly prepared 1-methylcyclotetramethylenearsine (I, R = CH_3). This arsine readily combines with one molecular equivalent of chlorine to give the arsine dichloride, a white solid which melts at 112–115° and which, when heated under reduced pressure, loses methyl chloride with the formation of 1-chlorocyclotetramethylenearsine (I, R = Cl). This method of replacing a methyl group directly joined to the arsenic atom of a tertiary arsine by a chloro group has been frequently employed, as in the cyclopentamethylenearsines (p. 38), the tetrahydroarsinolines (p. 43), and the tetrahydroisoarsinolines (p. 45).

Arsindoles

These compounds, which have the general formula (IV), R.I. 795, where R may be an alkyl, aryl, or halogeno group, are of very considerable interest because they represent the arsenic analog of indole, and constitute one of the very few systems in which arsenic forms part of a "semiaromatic" ring. It is clear, however—on the basis of recorded work—that the factors (mainly those of resonance), which stabilize the pyrrole and indole rings and render their nitrogen atoms extremely inert, do not in the arsindoles similarly inactivate the arsenic atom, for in many arsindoles this atom appears to have almost the normal reactivity of a tertiary arsine group.

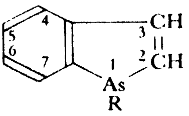
The first compound of this series was synthesized by Mannich,[18] who showed that 1-phenyl-2(diethylaminomethyl)acetylene, $C_6H_5C:C·CH_2N(C_2H_5)_2$, reacted with arsenic trichloride at 150–170° to give 1,3-dichloro-2(diethylaminomethyl)arsindole (V). This compound, by virtue of its tertiary amine group, forms a hydrochloride, m.p. 199°. The chloro group in the 1 position is (as expected) more reactive than that in the 3 position: the compound when treated with the appropriate acid therefore forms the 1-bromo-3-chlorohydrobromide, decomp. 205°, and the 1-iodo-3-chloro hydriodide, decomp. 194.5°: it will also give the 1-hydroxy-3-chloro hydrochloride, m.p. 135°. Aqueous potassium cyanide reacts with the original hydrochloride to give 1-cyano-3-chloro-2-(diethylaminomethyl)arsindole, m.p. 65°.

---

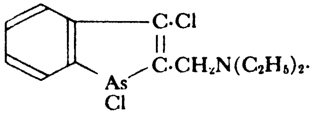
[16] H. N. Das-Gupta, *J. Indian Chem. Soc.*, **15**, 498 (1938).

[17] Steinkopf, Schubert, and Roch, *Ber.*, **65**, 409 (1932).

[18] Mannich, *Arch. Pharm.*, **273**, 275 (1935).

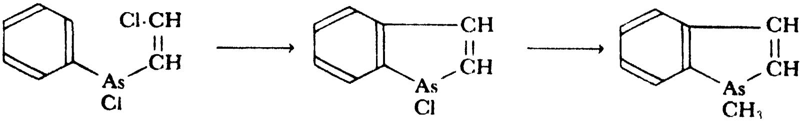


(IV)



(V)

A number of other syntheses of the arsindole ring system have been claimed by Das-Gupta. This author[19,20] has shown that phenyl-2-chlorovinylchloroarsine (VI), obtained by the interaction of 2-chlorovinyldi-



(VI) (VII) (VIII)

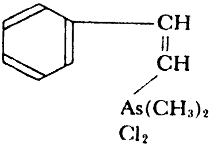
chloroarsine and benzene, undergoes cyclization when boiled in carbon disulfide solution with aluminum chloride for 7 hours, with the formation of 1-chloroarsindole (VII). It is claimed that the latter can also be obtained by cyclization of *o*-vinylphenyldichloroarsine, $CH_2:CH·C_6H_4·AsCl_2$. 1-Chloroarsindole, when treated with magnesium methyl iodide, gives 1-

---

[19] H. N. Das-Gupta, *J. Indian Chem. Soc.*, **12**, 627 (1935).
[20] H. N. Das-Gupta, *J. Indian Chem. Soc.*, **14**, 231, 349 (1937).

methylarsindole (VIII), a colorless liquid, b. p. 142–145°/6 mm. The reactivity of the arsenic atom in this compound is shown by the fact that it gives a quaternary methiodide, decomp. 216–218°, and a mercurichloride, m.p. 150–151°, and a picrate, m.p. 106–107°. 1-Ethylarsindole was similarly obtained as a liquid, b.p. 138–145°/6 mm.; it gave a picrate, m.p. 100–102°. Both 1-methyl- and 1-ethylarsindole are described as having offensive odors and vesicant action.

In an entirely different type of synthesis[21], dimethylstyrylarsine, $C_6H_5CH{:}CHAs(CH_3)_2$, was treated with chlorine in carbon tetrachloride solution, and the product when evaporated in vacuum and heated at 185–190° yielded 1-methylarsindole. It is clear that in these circumstances the tertiary arsine first formed the dichloride (IX), which when on heating



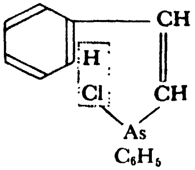
(IX)

lost methyl chloride, and also hydrogen chloride on cyclization, to give the 1-methylarsindole: the synthesis is thus a direct application of Turner and Bury's much earlier synthesis[22] of 1-methylarsindoline (see later). In another synthesis[23] 2-bromostyrene was heated with arsenic trichloride and sodium in benzene containing ethyl acetate to give tris(2-phenylvinyl)arsine, $(C_6H_5{\cdot}CH{:}CH)_3As$, m.p. 82°: this compound when heated with more arsenic chloride was supposed to give an unstable 2-phenylvinyldichloroarsine, $C_6H_5{\cdot}CH{:}CHAsCl_2$, which on further heating then lost hydrogen chloride during cyclization to form 2-chloroarsindole (VII).

It is also claimed[21] that a mixture of 2-bromostyrene and phenyldichloroarsine—when dissolved in ethanolic 33% sodium hydroxide solution, and first kept at room temperature for 24 hours, then heated on a water bath for 10 hours and finally reduced by sulfur dioxide in the presence of hydrochloric acid— ultimately gave 1-phenylarsindole, b.p. 165–170°/3 mm. It is clear that in these circumstances the bromostyrene has reacted with the phenyldichloroarsine by a Meyer reaction to give phenyl-(2-phenylvinyl)arsinic acid, $C_6H_5(C_6H_5CH:CH)AsO(OH)$, and that the latter has then been reduced to phenyl-(2-phenylvinyl)-chloroarsine (X).

---

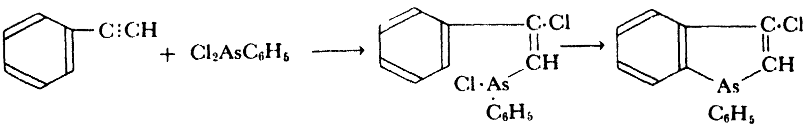
[21] H. N. Das-Gupta, *J. Indian Chem. Soc.*, **14**, 397, 400 (1937).
[22] Turner and Bury, *J. Chem. Soc.*, **123**, 2489 (1923).
[23] H. N. Das-Gupta, *J. Indian Chem. Soc.*, **15**, 495 (1938).



(X)

An unusually ready cyclization with loss of hydrogen chloride must now have occurred, as shown, to form 1-phenylarsindole.

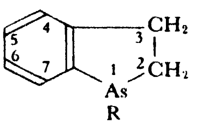
Finally, Das-Gupta[23] has shown that when phenylacetylene and phenyldichloroarsine are heated together at 140–150° for 7 hours, condensation occurs with the evolution of hydrogen chloride and the formation of 3-chloro-1-phenylarsindole (XII), with the probable intermediate formation of phenyl-(2-phenyl-2-chlorovinyl)chloroarsine (XI). The 3-chloro-1-phenylarsindole (XII) is thus obtained as a colorless liquid, b.p. 165–175°/10 mm.: it forms a picrate, m.p. 115–116°, and a mercurichloride, m.p. 232–235°, and also the following quaternary salts: methiodide, m.p. 152–153°; ethiodide, m.p. 161°. Evidence for the structure (XII) is obtained from the fact that oxidation with hydrogen peroxide breaks the heterocyclic ring, with the formation of *o*-carboxydiphenylarsinic acid, $C_6H_5(C_6H_4 \cdot COOH)AsO(OH)$, m.p. 165°.



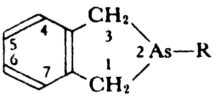
(XI) (XII)

Arsindolines and Isoarsindolines

It will be seen from the above that the existence of the arsenic analogs of indole appears to be well established: on the other hand, it is not surprising that the arsenic analogs of isoindole, like isoindole itself, are unknown, The dihydro derivatives of both classes of arsenic compound are known, however. They are the arsindolines or dihydroarsindoles, of general



(I)

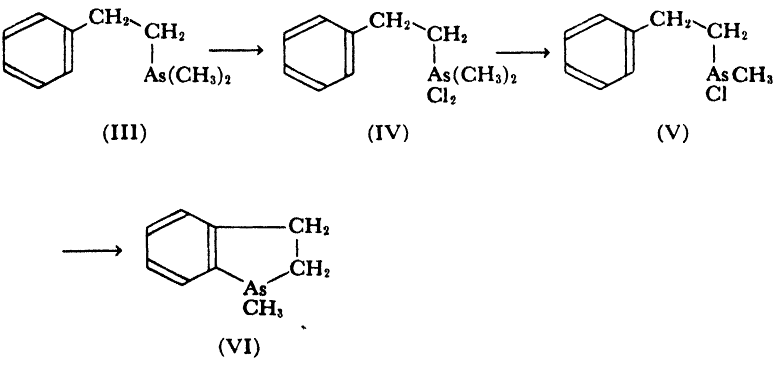


(II)

formula (I), and the isoarsindolines or dihydroisoarsindoles, of general formula (II). As in the case of so many heterocyclic arsenic derivatives, the true parent compounds in which R = H are unknown, and only derivatives in which R represents an alkyl, aryl, or halogen group, etc., have been isolated.

Arsindolines

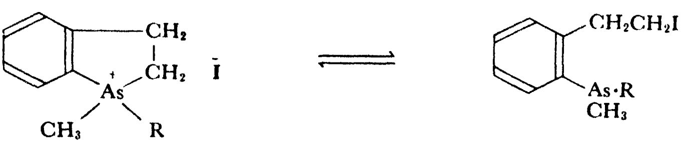
Only one member of this series appears to be known. It has been shown by Turner and Bury[22] that when the Grignard reagent prepared from 2-phenylethyl bromide, *i.e.*, $C_6H_5CH_2CH_2MgBr$, is treated with di-



(III) (IV) (V)

(VI)

methyliodoarsine, $(CH_3)_2AsI$, dimethyl-2-phenylethylarsine (III) is obtained. This arsine adds on chlorine to give the dichloride (IV), which on heating loses methyl chloride to form methyl-2-phenylethylchloroarsine (V). The latter compound, when gently warmed in carbon disulfide solution with aluminum chloride, cyclizes with loss of hydrogen chloride to give 1-methyl-(or As-methyl)-arsindoline (VI), a colorless liquid, b.p. 112–113°/15 mm. This arsindoline has, as would be expected, the normal properties of a tertiary arsine, and gives the following quaternary salts, all of which form colorless crystals: methiodide, m.p. 250°; ethiodide, m.p. 162–163°; benzyl bromide, m.p. 180°. Ethanolic solutions of the methiodide and ethiodide are colorless when cold, but develop a brown coloration when warmed: since this change is reversed on cooling, Turner and Bury[22] suggest that the quaternary salt (VII) in solution may be in equilibrium with the tertiary arsine (VIII). Heat shifts the equilibrium point from left to right, but on cooling again, this point must move almost entirely back to the left, judging from the apparently complete decolorization that occurs.

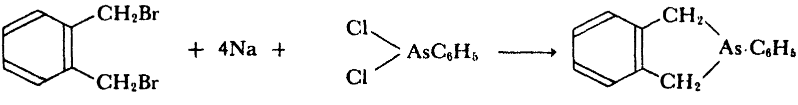


(VII) (VIII)

Isoarsindolines

The preparation and properties of these compounds have been examined in some detail. They may be prepared in three ways.

(*1*) Lyon and Mann[24] have shown that when *o*-xylylene dibromide (I) and, for example, phenyldichloroarsine, are boiled together in ethereal



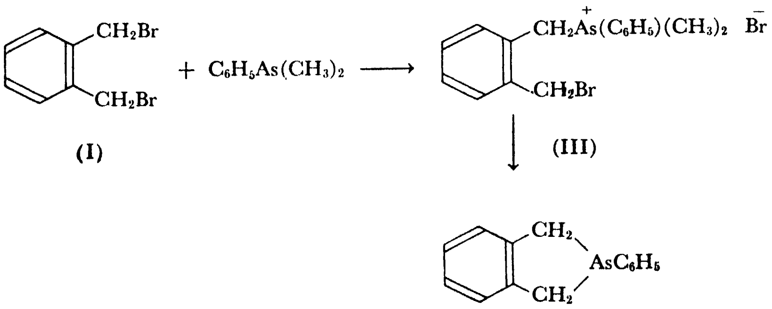
(I) (II)

---

[24] Lyon and Mann, *J. Chem. Soc.*, **1945**, 30.

solution with sodium and a small quantity of ethyl acetate under an atmosphere of nitrogen, direct condensation occurs with the formation of 2-phenylisoarsindoline (II). Several such compounds have been prepared by this method.

(*2*) The second method, of Lyon, Mann and Cookson,[25] is much less troublesome, since the long boiling under nitrogen and the distillation of the ether are completely avoided. In this method, equimolecular quantities of *o*-xylylene dibromide (I) and, for example, dimethylphenylarsine are mixed and warmed. Immediate reaction occurs with the formation of a number of compounds, one of which is almost certainly the quaternary arsonium salt (III). When this crude product is heated in a vacuum



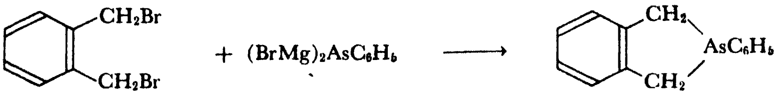
(I)

(III)

(II)

methyl bromide is lost as cyclization occurs, and the 2-phenylisoarsindoline then distils over. The method is rapid and the yield comparatively high.

(*3*) When the di-Grignard reagent[26] prepared from phenylarsine, $C_6H_5AsH_2$, *i.e.*, the reagent $C_6H_5As(MgBr)_2$, is treated with *o*-xylylene dibromide, a rapid reaction occurs with the formation of 2-phenyliso-



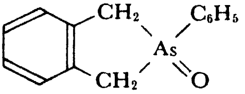
(II)

---

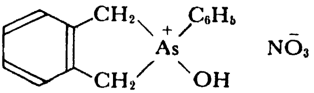
[25] Lyon, Mann, and G. H. Cookson, *J. Chem. Soc.*, **1947**, 662.
[26] Beeby, G. H. Cookson, and Mann, *unpublished work.*

arsindoline. This method could clearly be of considerable value, and it yields a product of high initial purity.

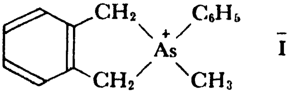
The 2-alkyl- and the lower 2-arylisoarsindolines thus prepared are liquids at room temperature, but the higher 2-aryl derivatives are crystalline. They possess many of the properties of stable tertiary arsines. For example, when the 2-phenylisoarsindoline is oxidized with nitric acid, it forms the oxide (IV), but the highly polar As—O group causes this compound to form the crystalline hydroxy nitrate (V), which, systematically, should be termed 2-hydroxy-2-phenylisoarsindolinium nitrate. These hydroxy nitrates are of course ionized salts and when treated with, for example, picric acid give the corresponding hydroxy picrates. The hydroxy nitrates are often of considerable value as a means of purifying the crude tertiary arsines, for the hydroxy nitrates themselves can usually be readily purified by recrystallization from water or dilute nitric acid, and then on treatment with alkali give the arsine oxide (IV), which in turn can be expeditiously reduced in chloroform solution by sulfur dioxide to the pure tertiary isoarsindoline. The isoarsindolines also readily form quaternary salts with alkyl iodides: 2-phenylisoarsindoline thus gives the methiodide (VI), *i.e.*, 2-methyl-2-phenylisoarsindolinium iodide, which in turn can also be converted to the corresponding picrate. The properties of a number of the isoarsindolines and their chief derivatives are summarized in Table I.



(IV)



(V)



(VI)

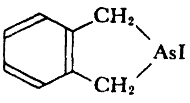
It is noteworthy that 2-phenylisoarsindoline oxide, (IV), and therefore also the dihydroxide which it readily forms in presence of water, shows marked activity against *Trypanosoma congolense* in mice, but very little activity against *Trypanosoma rhodesiense* and *Trypanosoma cruzi*: replacement of the 2-phenyl group by the other aryl groups listed in the Table I does not affect these comparative activities.

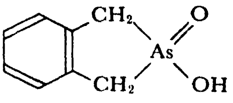
TABLE I. 2-Substituted Isoarsindolines[a]

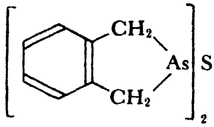
2-Substituent	Arsine		Oxide, m.p., ° C.	Hydroxy nitrate, m.p., ° C.	Hydroxy picrate, m.p., ° C.	Meth-iodide, m.p., ° C.	Methopic-rate, m.p.
	M.p., ° C.	B.p., ° C./mm.					
CH_3	Liquid	115/17	—	—	—	—	—
C_6H_5	Liquid	136–138/ 0.3	130–131	149–150	164–166	—	—
p-$CH_3.C_6H_4$	Liquid	138–139/ 0.3	134–136	146	147	156	134–135
p-ClC_6H_4	63–64	153–154/ 0.05	145–146	144–145	147–148	204	162
p-$CH_3O.C_6H_4$	69–70[b] 91–92	167–168/ 0.03	150–151	141	159	148	134

[a] *Note*: Many of the above melting points are affected by the time of heating during the determination.
[b] Dimorphous.

The heterocyclic ring in the isoarsindolines has remarkable stability. When the above 2-aryl derivatives are heated with an excess of aqueous hydriodic acid of constant boiling point, the aryl group is split off, and the highly crystalline yellow 2-iodoisoarsindoline (VII), m.p. 107–108°, is obtained. By the application of a suitable Grignard reagent, the 2-iodo group can now be replaced by any desired alkyl or aryl group, and the iodo compound (VII) is therefore a valuable intermediate in converting one 2-substituted isoarsindoline into another. When 2-iodoisoarsindoline is treated first with sodium carbonate solution and then with hydrochloric acid, the 2-chloroisoarsindoline is obtained as colorless crystals, m.p. 73–74°. Oxidation of the 2-iodo compound with nitric acid yields *o*-xylylene-

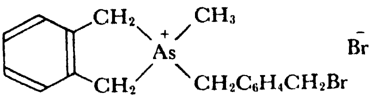

(VII)


(VIII)

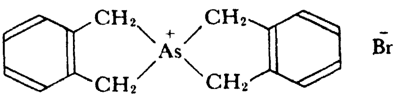

(IX)

arsinic acid (VIII), which separates from solution as the crystalline dihydroxy nitrate: treatment of the latter with one equivalent of alkali liberates the arsinic acid (VIII), colorless crystals, m.p. 144°. Furthermore, when the 2-iodo compound (VII) is hydrolyzed with sodium hydroxide, and the product treated with hydrogen sulfide, bis-2-isoarsindolyl sulfide (IX) is obtained as magnificent white crystals, m.p. 146°. It will be seen, therefore, that the heterocyclic ring has remained unchanged both in the formation of the 2-iodo derivative, and in all the subsequent reactions of this compound noted above: in particular, it is unaffected by such vigorous reducing and oxidizing agents as hydriodic acid and nitric acid, respectively.

The reactions of the isoarsindolines have provided the first synthetic approach to the spirocyclic arsonium salts in which the arsenic atom is linked by all its four covalencies to carbon atoms. Lyon and Mann[24] have shown that 2-methylisoarsindoline combines readily with one molecular equivalent of *o*-xylylene dibromide to give 2-*o*-(bromomethyl)-benzyl-2-methylisoarsindolinium bromide (X), which on heating in a



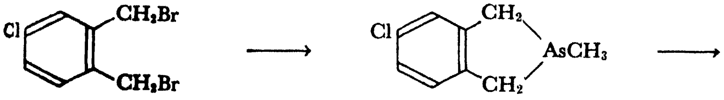
(X)



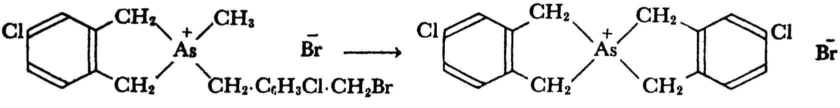
(XI)

vacuum loses methyl bromide to form *As-spiro*-bis-isoarsindolinium bromide (XI). This salt, and the corresponding iodide and picrate, form extremely beautiful crystals.

Since the 4-covalent arsonium atom is known to have a tetrahedral configuration, it follows that if a spirocyclic arsonium salt similar to (XI) but having a suitable substituent in the benzene rings were prepared, it would possess molecular dissymmetry and hence should be susceptible to resolution into optically active forms. Lyon, Mann, and Cookson[25] therefore converted 4-chloro-*o*-xylylene dibromide (XII) into 5-chloro-2-methylisoarsindoline (XIII), which in turn was combined with a second equivalent of the dibromide (XII) to form the arsonium salt (XIV). The latter, when heated at 160–170°/15 mm., readily lost methyl bromide with the formation of the highly crystalline *As-spiro*-bis-5-chloroisoarsindolinium bromide (XV). This salt must clearly lack any elements of symmetry, although the arsenic atom is not asymmetric. Yet, although a number of salts with optically active acid radicals were prepared and examined, no decisive evidence of optical resolution was obtained. This result is in striking contrast to the ready resolution of another spirocyclic salt, *As-spiro*-bis-1,2,3,4-tetrahydroisoarsinolinium bromide, by Holliman and Mann[27] (see p. 49).



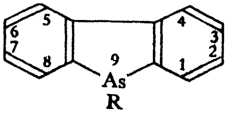
(XII) (XIII)



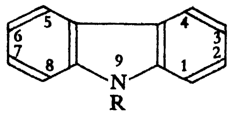
(XIV) (XV)

Arsafluorenes or 2,3-Benzarsindoles

These compounds have the general formula (I), R.I. 1620, and they are clearly, therefore, the arsenic analogs of the corresponding carbazoles (II): consequently it is desirable that the numbering of the ring system in the arsenic compounds (I) should correspond with that commonly accepted for carbazole and its derivatives, which is given in formula (II). There is some difficulty, however, in choosing a suitable name for the ring system shown in (I). Compounds of this type were discovered by Aeschlimann, Lees, McCleland, and Nicklin,[28] who termed them "*o,o′*-diphenylylene-



(I)



(II)

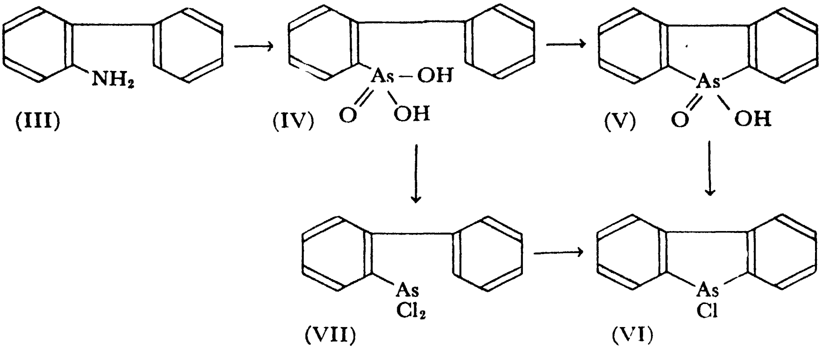
---

[27] Holliman and Mann, *J. Chem. Soc.*, **1945**, 45.

[28] Aeschlimann, Lees, McCleland, and Nicklin, *J. Chem. Soc.*, **127**, 66 (1925).

arsines": this would be modernized to "2,2′-biphenylylenearsines," but this name introduces an entirely different numbering to the system (I). The same objection applies to the term "2,3-benzarsindole": this term is systematically correct, but introduces yet another system of numbering. The term "arsa-carbazole" is unsatisfactory, since it implies that the compounds contain both arsenic and nitrogen. The term "arsa-fluorene" has therefore been adopted in the present work, the compounds being regarded as fluorene with the $\diagdown \mathrm{CH_2} \diagup$ group replaced by the $\diagdown \mathrm{AsH} \diagup$ group in the parent member of the arsafluorene series: the numbering given in (I) can then be adopted, and the compounds fall into line with their carbazole analogs.

Aeschlimann and coworkers[28] have shown that 2-aminobiphenyl (III), when subjected to the usual Bart reaction, furnishes biphenylyl-2-



arsonic acid (IV), which when heated with sulfuric acid at 100° for a few minutes readily cyclizes to the arsinic acid (V), colorless crystals, m.p. 290°. (If the term "arsafluorene" is adopted, this acid will presumably be named "arsafluorinic acid.") This arsinic acid, when subjected to the usual reduction with sulfur dioxide in the presence of hydrochloric acid, gives 9-chloro- (or As-chloro)-arsafluorene (VI), colorless crystals, m.p. 161°, b.p. approx. 230°/25 mm. Alternatively, the arsonic acid (IV) can be similarly reduced to 2-biphenylyldichloroarsine (VII), a heavy oil which when heated in a vacuum cyclizes with loss of hydrogen chloride also to give the 9-chloro derivative (VI).

It should be noted that Aeschlimann *et al.*[28] give no specific directions for the conversion of 2-aminobiphenyl (III) to the biphenylyl-2-arsonic acid (IV). These have recently been given by Cookson and Mann,[28a] who also described the reduction to 2-biphenylyldichloroarsine (VII), which they have obtained as colorless crystals, m.p. 47.5–48.5°.

9-Chloroarsafluorene (VI) has the normal properties associated with a diaryl monochloroarsine. For example, it can be converted to the 9-iodo compound (I, R = I), golden plates, m.p. 166°, and to the 9-cyano compound (I, R = CN), white needles, m.p. 178°. When hydrolyzed, the chloro compound furnishes the diarsine oxide, $C_{12}H_8As{\cdot}O{\cdot}AsC_{12}H_8$, white crystals, also having m.p. 178°. Magnesium methyl iodide converts the 9-chloro compound to the tertiary arsine, 9-methylarsafluorene (I, R = CH_3): this compound has been isolated as large prisms, m.p. 46 °, having a pleasant orange-like odor. Although completely satisfactory analyses have not been obtained with this compound, its identity is reasonably certain, particularly as it combines with methyl iodide to give a pure crystalline methiodide (systematically named 9,9 dimethylarsafluorenonium iodide), m.p. 190°. It is noteworthy that the corresponding *N*-methylcarbazole does not form a quaternary methiodide. This example illustrates further the fact already mentioned in connection with the arsindoles (p. 26), that when arsenic replaces nitrogen in a pyrrole ring it does not acquire thereby the very low activity of the nitrogen atom.

Six-Membered Ring Systems Containing Only Carbon and Arsenic

Cyclopentamethylenearsines

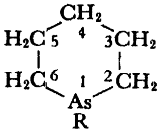
These arsines have the general formula (I), R.I. 196, and the ring is numbered as indicated. The first members were prepared by Grüttner and Wiernik,[29] who isolated the 1-phenyl and 1-*p*-tolyl members: shortly after, Zappi prepared the 1-methyl member. Zappi[30] has suggested that the unknown arsenic analog (II) of pyridine should be termed *arsedine* and the arsenic analog (III) of piperidine should be termed *arsepidine*: the parent compound (III) is also unknown, although many derivatives have been prepared. The name arsepidine apparently has not been adopted by the German workers.

[28a] G. H. Cookson and Mann, *J. Chem. Soc.*, **1949**, 2897.

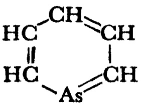
[29] Grüttner and Wiernik, *Ber.*, **48**, 1473 (1915).

[30] Zappi, *Bull. soc. chim. France* [IV], **19**, 151, 290 (1916).

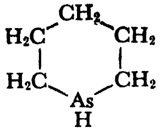
Grüttner and Wiernik[29] prepared 1-phenyl (or As-phenyl)cyclopentamethylenearsine (I, R = C_6H_5) by the interaction of the di-Grignard reagent prepared from 1,5-dibromo-*n*-pentane, *i.e.*, $CH_2(CH_2CH_2MgBr)_2$,



(I)



(II)



(III)

and phenyldichloroarsine: the *p*-tolyl analog was similarly prepared using *p*-tolyldichloroarsine. They also prepared the 1-phenyl compound by the interaction of 1,5-dibromo-*n*-pentane, phenyldichloroarsine, and sodium, but found this method inferior to that described above. Zappi[30] has prepared the 1-methyl compound (I, R = CH_3) by the action of the above di-Grignard reagent on methyldichloroarsine, and Steinkopf, Donat, and Jaeger[31] have similarly prepared the 1-ethyl compound (I, R = C_2H_5).

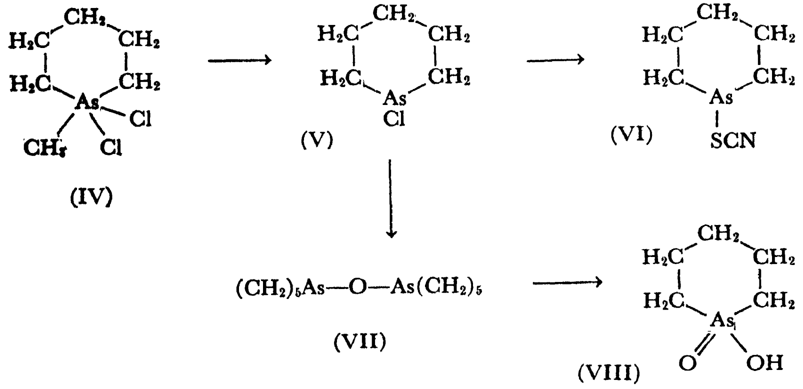
The properties of the various homologs will be discussed briefly in ascending order.

The 1-methyl compound[30] is a colorless liquid, b.p. 156°/760 mm., 76°/36 mm., and 65°/20–22 mm., *D* 1.218. It is volatile in steam, smells like oil of mustard, and is readily oxidized in air. It unites with methyl iodide to give a methiodide (systematically named 1,1-dimethylcyclopentamethylenearsonium iodide), white crystals which when heated in a sealed tube melt at 290°, but when heated in the open dissociate to the original arsine and methyl iodide. The methiodide gives a methopicrate, yellow crystals, m.p. 258°.

The methyl arsine, like most tertiary arsines, readily combines with halogens. Zappi[30] states that it unites with chlorine to give a dichloride (IV) as a hygroscopic viscous mass, which in a vacuum gave methyl chloride and 1,5-dichloro-*n*-pentane. Steinkopf, Schubert, and Roch[17] state, however, that this dichloride, on heating to about 166°, loses methyl chloride to form 1-chlorocyclopentamethylenearsine (V), a liquid of b.p. 84–86°/13 mm., the constitution of which was confirmed by the fact that it reacted with sodium thiocyanate to give the 1-thiocyanato analog (VI).

[31] Steinkopf, Donat, and Jaeger, *Ber.*, **55**, 2610 (1922).

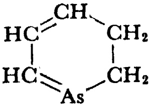
The production of the 1-chloroarsine (V) has been confirmed by Gorski, Schipanski, and Muljav,[32] who have shown that on treatment with sodium methoxide in methanol it gives the diarsine oxide (VII), which on oxidation with hydrogen peroxide forms cyclopentamethylenearsinic acid (VIII), colorless crystals, m.p. 200.5–202 °. It is probable that Zappi's observation regarding the dissociation of the dichloride (IV) was incorrect, for he states in the same paper[30] that the 1-methyl arsine adds on bromine to give a very hygroscopic dibromide which decomposes on heating to form methyl bromide and 1-bromocyclopentamethylenearsine (I, R = Br). The 1-methylarsine also adds on iodine to give a di-iodide[30]; this apparently differs in physical properties from the corresponding dichloride and dibromide, as it forms a yellow powder, m.p. 120 °, with decomposition. Much later, Zappi and Degiorgi[33] stated that the 1-methylarsine (I, R = CH_3) reacts in cold carbon tetrachloride solution with one atomic proportion of bromine to give a compound formulated as $[(CH_2)_5As(CH_3)Br]_2$, very hygroscopic white crystals, m.p. 60°: this compound when exposed to air gives a peroxide, and when treated with more bromine gives the above dibromide. In this paper,[33] the thermal dissociation of the dibromide when heated at 80–90°/6–8 mm. to give methyl bromide and the 1-bromoarsine (I, R = Br) is confirmed. It is also shown that the 1-bromoarsine, which is a red oil, combines with a further molec-



---

[32] Gorski, Schipanski, and Muljav, *Ber.*, **61**, 730 (1934).
[33] Zappi and Degiorgi, *Bull. soc. chim. France* [IV], **49**, 366 (1931).

ular equivalent of bromine to form 1,1,1-tribromocyclopentamethylenearsine, colorless crystals, m.p. 102°. This tribomide when treated with water forms hydrogen bromide and the arsinic acid (VIII); when heated, however, it gives gaseous hydrocarbons and arsenic tribromide, and not the dihydroarsedine (IX) as these authors had hoped.



(IX)

1,2-Dimethylcyclopentamethylenearsine[34] has been prepared by the action of methyldichloroarsine on the di-Grignard reagent prepared from 1,5-dichloro-*n*-hexane, $Cl(CH_2)_4CH(CH_3)Cl$. It is a liquid, b.p. 169°/760 mm., 85°/22 mm.: it forms a methiodide which sublimes at 340° in a sealed tube, a methochloride and a methopicrate, m.p. 231° (decomp.). The arsine oxide, when exposed to the air, and when treated in ligroin solution with iodine, is stated to form a resin.

1-Ethylcyclopentamethylenearsine[31] (I, R = C_2H_5) is a liquid, b.p. 62–64°/12.5 mm., which forms a methiodide, m.p. 276°. It combines with cyanogen bromide to give a very deliquescent addition product, which is readily hydrolyzed to the hydroxy bromide, m.p. 71°, and which when heated gives rise to various products, among which the original ethylarsine, cyanogen bromide, and ethyl bromide have been identified.

The 1-chlorovinylhomolog[32] (I, R = ClCH:CH.) has been prepared by the action of the usual di-Grignard reagent on 2-chlorovinyldichloroarsine. It is a colorless liquid, b.p. 89–91°/5 mm., which gives a crystalline dichloride, m.p. 121°. The thermal dissociation products of this dichloride have been investigated.

1-Phenylcyclopentamethylenearsine[29] is a colorless, rather viscous oil, b.p. 153–154°/18–20 mm., which has a feeble odor and is not markedly oxidized in air. It forms a dichloride, colorless, very deliquescent, crystals, m.p. 138–139°, which on heating decompose giving 1,5-dichloro-*n*-pentane. It also forms a mercuri-chloride, colorless crystals of composition $C_{11}H_{15}As{\cdot}HgCl_2$, m.p. 201.5–202°. A number of quaternary salts have been prepared: methiodide, m.p. 179.5°; ethiodide, m.p. 185°; *n*-propyl iodide, m.p. 137–138°, isopropyl iodide, m.p. not recorded; *n*-primary butyl iodide, m.p. 140°. This arsine, like the above 1-ethyl homolog, gives a cyanogen bromide addition product,[35] a white crystalline material, m.p. 107°, which is readily hydrolyzed to the hydroxy bromide, m.p. 162.5°, and which when heated under reduced pressure gives rise to a number of products including the original tertiary arsine. Steinkopf[31,35] and his co-workers conclude from these reactions that the cyclopentamethylenearsine ring system shows a greater stability towards cyanogen bromide than does the piperidine system.

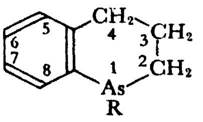
---

[34] Zappi and Simonin, *Ciencia Mex.*, **3**, 160 (1942).

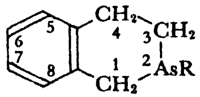
1-*p*-Tolylcyclopentamethylenearsine[29] is a colorless oil, b.p. 162–163°/20 mm., 177–178°/50 mm., which gives a dichloride, m.p. 134°, and a mercuri-chloride, m.p. 175°, similar in composition to that noted above. 2-Methyl-1-phenylcyclopentamethylenearsine[36] has also been described.

Tetrahydroarsinolines and Tetrahydroisoarsinolines

The terms arsinoline and isoarsinoline are applied to the compounds corresponding to quinoline and isoquinoline, respectively, in which the nitrogen atom has been replaced by arsenic. However, both these arsenic analogs are still unknown. Their 1,2,3,4-tetrahydro derivatives, having the general formulas (I), R.I. 1003, and (II) and corresponding to derivatives of 1,2,3,4-tetrahydroquinoline and 1,2,3,4-tetrahydroisoquinoline, respectively, are known. The numbering of the ring systems in these compounds shown in (I) and (II) is identical with that in their quinoline and isoquinoline analogs.



(I)



(II)

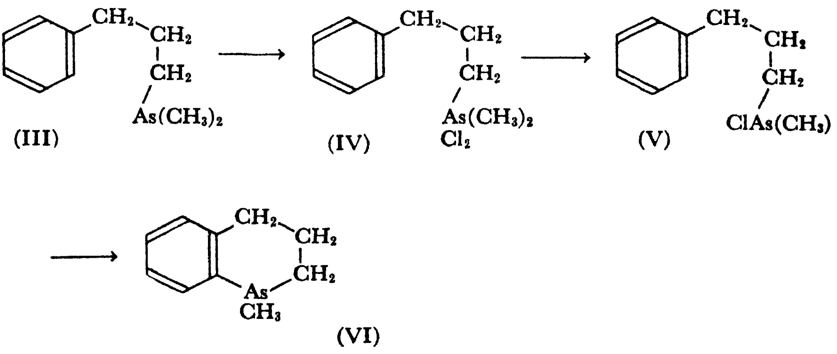
---

[35] Steinkopf and Wolfram, *Ber.*, 54, 848 (1921).
[36] German Pat. 313,876 (1919).

1,2,3,4-Tetrahydroarsinolines

Compounds of this class were first prepared by Burrows and Turner,[37] using a method of synthesis virtually identical with that later employed by Turner and Bury[22] for the preparation of 1-alkylarsindolines (p. 30). For the arsinoline synthesis, 3-phenylpropyl bromide, $C_6H_5(CH_2)_3Br$, was converted to the corresponding Grignard reagent, which when treated with dimethyliodoarsine, $(CH_3)_2AsI$, gave dimethyl(3-phenylpropyl)arsine (III), a colorless liquid, b.p. 133°/14 mm. This tertiary arsine was characterized by the preparation of its quaternary methiodide, m.p. 144°. The tertiary arsine (III), however, showed one unusual property in that it readily gave an additive compound with an equimolecular proportion of dimethyliodoarsine, this additive compound, which consequently had the composition $C_{11}H_{17}As,(CH_3)_2AsI$, formed colorless prisms, m.p. 78–81°, which could be recrystallized from a number of solvents. Molecular weight determinations in benzene solution, however, showed that it was completely dissociated into its components in this solvent.

The arsine (III) was converted in carbon tetrachloride solution to the arsine dichloride (IV), which when heated at 160–180° lost methyl chloride, giving methyl(3-phenylpropyl)monochloroarsine (V), a colorless liquid, b.p. 164–167°/14 mm. The monobromoarsine, b.p. 177–180°/16 mm., corresponding to (V), was prepared similarly. When the



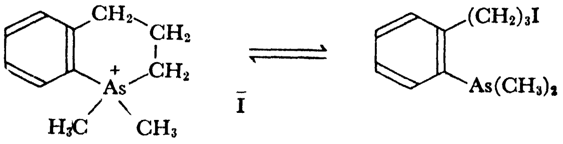
(III) (IV) (V) (VI)

---

[37] Burrows and Turner, *J. Chem. Soc.*, **119**, 430 (1921).

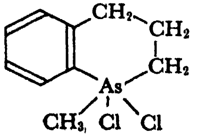
monochloroarsine (V) was boiled gently in carbon disulfide solution with aluminum chloride for three hours, cyclization occurred with loss of hydrogen chloride and the formation of 1-methyl-1,2,3,4-tetrahydroarsinoline (VI), a highly refractive liquid, b.p. 140°/14 mm. This arsine has a faint odor suggestive of quinoline and is oxidized slowly on exposure to the air.

The 1-methylarsinoline readily gives a quaternary methiodide (1,1-dimethyl-1,2,3,4-tetrahydroarsinolinium iodide) (VII), which forms colorless crystals, m.p. 235°. When dissolved in cold ethanol, this iodide gives a colorless solution, which, however, becomes yellow on heating: cooling the solution reverses this color change. Moreover, a rapid volumetric estimation of the ionic iodine in the pure salt (VII) in cold dilute ethanolic solution gave values about 7% lower than those obtained by the usual analytical methods. In view of these facts, Burrows and Turner[37] consider that the methiodide (VII) in solution is in equilibrium with the *o*-(3-iodopropylphenyl)dimethylarsine (VIII). These results are closely similar to those subsequently observed by Turner and Bury[22] for similar salts in the arsindoline series (p. 31).

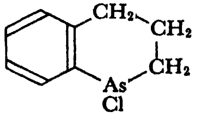


(VII) (VIII)

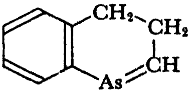
Roberts, Turner, and Bury[38] have shown that the 1-methylarsinoline (VI) will combine with chlorine to form the arsine dichloride (IX).



(IX)



(X)



(XI)

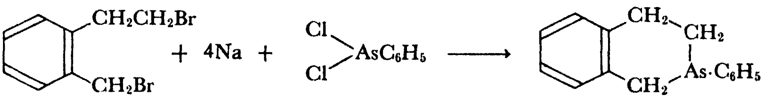
---

[38] Roberts, Turner, and Bury, *J. Chem. Soc.*, **1926**, 1443.

When this white solid addition product was heated under reduced pressure, methyl chloride was evolved smoothly with the formation of 1-chloro-1,2,3,4-tetrahydroarsinoline (X). Attempts to split off hydrogen chloride from the latter compound by boiling it with diethylaniline and so to obtain 3,4-dihydroarsinoline (XI) failed, and the latter compound is still unknown.

1,2,3,4-Tetrahydroisoarsinolines

Compounds of this class have been synthesized by Holliman and Mann,[39] using the *o*-(2-bromoethyl)benzyl bromide (XII) synthesized earlier by these workers.[40] The isoarsinoline synthesis is essentially the same as that used later by Lyon and Mann[24] for the preparation of 2-substituted isoarsindolines (p. 31). When an equimolecular mixture of the dibromide (XII) and phenyldichloroarsine in ethereal solution was boiled under an atmosphere of nitrogen for several hours with sodium wire and with occasional addition of small quantities of ethyl acetate, condensation occurred with the formation of 2-phenyl-1,2,3,4-tetrahydroisoarsinoline (XIII); the crude mixture was filtered while still under nitrogen, the ether then removed by distillation and the isoarsinoline (XIII) then obtained as a colorless liquid, b.p. 110–112°/0.01 mm. and 128–130°/0.05 mm. The use of methyldichloroarsine in the above synthesis similarly gave 2-methyl-1,2,3,4-tetrahydroisoarsinoline, b.p. 131°/18 mm.

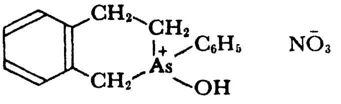


(XII) (XIII)

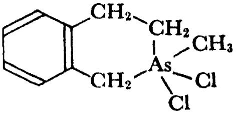
The heterocyclic ring in isoarsinolines of type (XIII) possesses considerable stability. When the 2-phenyl derivative (XIII) was treated with concentrated nitric acid, the hydroxy nitrate (XIV), *i.e.*, 2-hydroxy-2-phenyl-1,2,3,4-tetrahydroisoarsinolinium nitrate, was readily formed as colorless crystals. The 2-methyl analog underwent a similar oxidation. Furthermore, the 2-methyl analog combined readily with chlorine to form the white dichloride (XV), which when heated at 15 mm. pressure lost methyl chloride and furnished 2-chloro-1,2,3,4-tetrahydroisoarsinoline (XVI), a colorless liquid, b.p. 157°/14 mm. Following the work of Roberts, Turner, and Bury[38] on the isomeric chloroarsinoline (X), attempts were made to split hydrogen chloride from the 2-chloroisoarsinoline (XVI) by

---

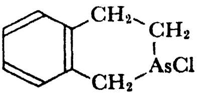
[39] Holliman and Mann, *J. Chem. Soc.*, **1943**, 547.
[40] Holliman and Mann, *J. Chem. Soc.*, **1942**, 737.



(XIV)



(XV)



(XVI)

boiling it in pyridine solution in order to form 3,4-dihydroisoarsinoline, but these attempts failed. It is noteworthy, however, that no fission of the heterocyclic ring was detected either in the above oxidation reactions or in the preparation and investigation of the 2-chloro derivative (XVI).

The reason for the failure to split off hydrogen chloride from the 2-chloroisoarsinoline (XVI) and for the similar earlier failure with 1-chloroarsinoline (X) is probably that the tetrahydro derivatives are much more stable than the 3,4-dihydro derivatives into which, therefore, they cannot be readily converted. The heterocyclic ring in the tetrahydro compounds is almost certainly "buckled" in order to avoid strain and so obtain maximum stability. The true arsinoline and isoarsinoline compounds if they were known, might be found to possess an enhanced stability owing to their "semi-aromatic" nature and to the consequent resonance. However, the intermediate 3,4-dihydro derivatives possess neither of these stabilizing factors and hence are difficult to isolate.

The properties of the chief derivatives of these two isoarsinolines are conveniently summarized in the Table II.

The stereochemical investigation of derivatives of the above isoarsinolines has led to novel results in two directions.

Many attempts by earlier workers had been made to resolve into optically active forms a quaternary arsonium salt of type [*abcd*As]X, where *a*, *b*, *c*, and *d* represent unlike groups and X is an acid radical. Partial success had been obtained only by Burrows and Turner,[37] and by Kamai,[41] but in each case these workers had succeeded solely in isolating an arsonium iodide of very low rotation, which, moreover, racemized rapidly in solution. Burrows and Turner attributed this failure to the fact that such quaternary arsonium iodides give rise in organic solvents to a "dissociation-equilibrium" of type $[abcd\text{As}]\text{I} \rightleftharpoons abc\text{As} + d\text{I}$. This equilibrium would of course cause rapid racemization, and since moreover all such arsonium salts investigated possessed (for synthetic reasons) at least one alkyl group attached to the arsenic atom, the formation of such a dissociation-equilibrium was always possible.

TABLE II. 2-Substituted Isoarsinolines

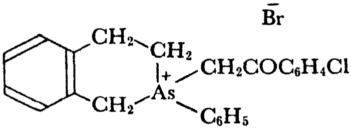
2-Substituent	Arsine, b.p., ° C./mm.	Hydroxy nitrate, m.p., ° C.	Hydroxy picrate, m.p., ° C.	Methiodide, m.p., ° C.	Methopicrate, m.p., ° C
CH_3	131/18	—	164–165.5	179–181	163–164
C_6H_5	110–112/0.01 128–130/0.05	149–150	116–118	136–137	—

Holliman and Mann had found, as shown above, that the heterocyclic ring in the tetrahydroisoarsinolines had very considerable stability. Moreover, there was evidence that if *p*-chlorophenacyl bromide, $ClC_6H_4COCH_2Br$, was used for quaternary salt formation, the *p*-chlorophenacyl group became linked to the arsenic atom very much more stably than an alkyl group; in effect it appeared to be as stably linked as an aryl group. Holliman and Mann[42] therefore combined the 2-phenylisoarsinoline (XIII) with *p*-chlorophenacyl bromide to give the quaternary salt 2-*p*-chlorophenacyl-2-phenyl-1,2,3,4-tetrahydroisoarsinolinium bromide (XVII) colorless crystals, m.p. 190–191°. This compound clearly con tains an asymmetric arsenic atom, and, on the basis of the above reason, should have great stability; in particular it should not undergo dissociation in solution. It was therefore converted into the *d*-bromocamphor sulfonate, which on repeated recrystallization from alcohol ultimately yielded the optically pure *l*-arsonium *d*-sulfonate. This salt was then converted by double decomposition into the *l*-2-*p*-chlorophenacyl-2-phenyl-1,2,3,4-tetrahydroisoarsinolinium iodide, $[M]_D$ −354° in chloroform solution, and the corresponding picrate, $[M]_D$ −450° in chloroform solution. Repetition of the resolution using the *l*-bromocamphor sulfonate similarly gave the *d*-picrate, $[M]_D$ + 457° also in chloroform solution. It is noteworthy that neither of these salts showed any perceptible racemization when left in chloroform solution at room temperature for several days: this high optical stability of the iodide, in particular, shows that no "dissociation-equilibrium" could have occurred in solution, although such equilibria occur more readily in chloroform than in any other common solvent. Salts of the cation shown in (XVII) therefore represent the only known example of an optically stable quaternary arsonium salt in which the optical activity is due to an asymmetric arsenic atom.

---

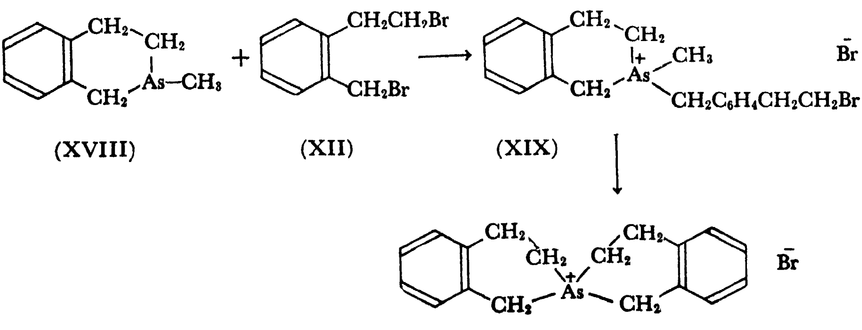
[41] Kamai, *Ber.*, **66**, 1779 (1933); *J. Gen. Chem. U.S.S.R.*, **4**, 184 (1934).

[42] Holliman and Mann, *J. Chem. Soc.*, **1943**, 550.



(XVII)

In a second direction, notable results were obtained by applying Lyon and Mann's spirocyclic arsonium salt synthesis,[24] to the corresponding isoarsinoline derivatives. For this purpose, Holliman and Mann[27] combined 2-methyl-1,2,3,4-tetrahydroisoarsinoline (XVIII) with an equimolecular quantity of the dibromide (XII) to form the arsonium salt (XIX). When this salt was heated at 14 mm. pressure, with the temperature ultimately rising to 200°, it lost methyl bromide with the formation of the spirocyclic salt, *As-spiro*-bis-1,2,3,4-tetrahydroisoarsinolinium bromide (XX). Since the 4-covalent arsenic atom is known to have a tetrahedral configuration, it follows that the two isoarsinoline ring systems in this compound are at right angles to one another. Consequently the compound possesses molecular dissymmetry, although the arsenic atom itself is symmetric. The bromide (XX) was therefore converted into the corresponding *d*-bromocamphor sulfonate, which on recrystallization from water ultimately furnished the optically pure *l*-isoarsinolinium *d*-sulfonate. This compound was then converted to the *l*-*As-spiro*-bis-1,2,3,4-tetrahydroisoarsinolinium iodide, which had $[M]_{\mathrm{D}} - 344^\circ$ in chloroform solution. The resolution was then repeated using the *l*-bromocamphor sulfonate, and the optically pure *d*-iodide, having $[M]_{\mathrm{D}} + 342^\circ$ in chloroform thus isolated. No racemization of these *d*- and *l*-iodides in chloroform solution at room temperature could be detected over a period of several days.

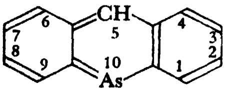

(XVIII) (XII) (XIX)

(XX)

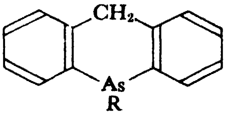
It is noteworthy that the molecular rotation of the iodide corresponding to the arsonium salt (XVII) and of that corresponding to the spirocyclic salt (XX) were determined for various wave lengths, and for approximately equimolecular solutions in chloroform these values were closely similar throughout, although the optical activity in (XVII) is due to the asymmetric arsenic atom and that in (XX) to molecular dissymmetry. This probably indicates that in both compounds the optical activity originates mainly in electronic transitions which are centered at the arsenic atom.

Arsacridines

The name arsacridine is given to the still undiscovered compound (I), R.I. 1940, which can be regarded as acridine, with the N atom replaced by arsenic (p.3). The compounds prepared in this field usually have the general formula (II), and hence are regarded as 10-substituted derivatives of 5,10-dihydroarsacridine.

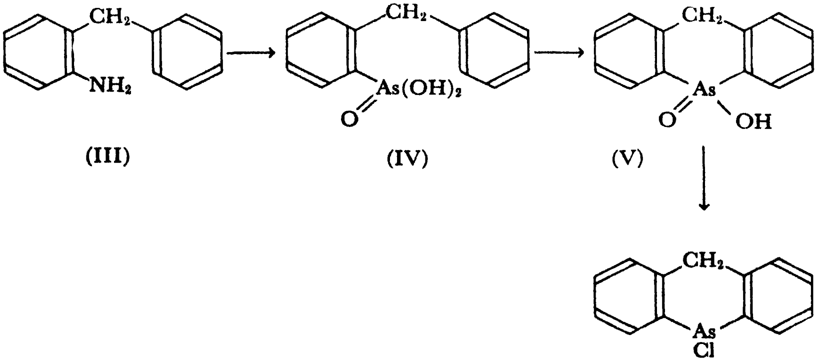


(I)



(II)

Compounds in this series were first synthesized by Gump and Stoltzenberg,[43] who converted 2-aminodiphenyl methane (III) by a Bart reaction to diphenylmethane-2-arsonic acid (IV), m.p. 161–162°. When this compound was heated with sulfuric acid at 100°, it underwent cyclization to give arsacridinic acid (V), m.p. 235–236°. This acid, when reduced



(III) (IV) (V) (VI)

with sulfur dioxide in the presence of hydrochloric acid, gave 10-chloro-5,10-dihydroarsacridine (VI), m.p. 114–115°. It should be noted that Gump and Stoltzenberg used the term "acridarsine" for the parent compound in this field and the term "arsacridine" was adopted later: consequently they term the acid (V) "acridarsinic acid."

The synthesis of various 2-aminodiphenylmethanes for subsequent cyclization by the Gump and Stoltzenberg method has been considerably improved by Todd *et al.*[44,45] By the use of these substituted 2-aminodiphenylmethanes, the following arsacridine derivatives were prepared (Table III).

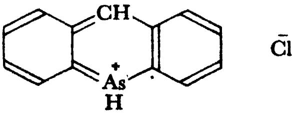
---

[43] Gump and Stoltzenberg, *J. Am. Chem. Soc.*, **53**, 1428 (1931).

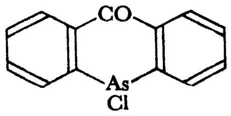
TABLE III

Arsacridine derivatives	M.p., ° C.
3-Methylarsacridinic acid	184 decomp.
3-Chloroarsacridinic acid	210–212 decomp.
10-Cyano-5,10-dihydroarsacridine	114–115
10-Chloro-2-methyl-5,10-dihydroarsacridine	65.5–66.5
10-Chloro-3-methyl-5,10-dihydroarsacridine	87
3,10-Dichloro-5,10-dihydroarsacridine	116
3-Chloro-10-cyano-5,10-dihydroarsacridine	113–114

Gump and Stoltzenberg,[43] following a parallel suggestion made by Kappelmeier[46] concerning the 5,10-dihydrophenarsazines, suggest that the 10-chloro compound (VI) may exist in the form of the arsonium salt (VII) "because it behaves like acridine in its skin-irritating properties." This can hardly be accepted as very weighty evidence, particularly since several diaryl monochloroarsines of type R^1R^2AsCl, in which such tautomerism is impossible, are known to have vesicant action on the skin.



(VII)



(VIII)

In view of the ease with which the arsacridine ring system can be synthesized, it is curious that the corresponding arsacridone derivatives are still unknown. Aeschlimann and McCleland[47] failed to prepare the

---

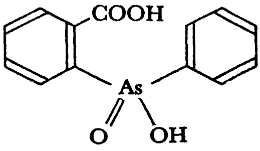
[44] Hewett, Lermit, Openshaw, Todd, Williams, and Woodward, *J. Chem. Soc.*, **1948**, 292.

[45] Davies, Openshaw, Spring, Stanley, and Todd, *J. Chem. Soc.*, **1948**, 295.

[46] Kappelmeier, *Rec. trav. chim.*, **49**, 57 (1930).

[47] Aeschlimann and McCleland, *J. Chem. Soc.*, **125**, 2025 (1924).

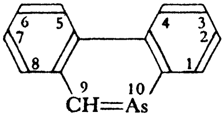
10-chloroarsacridone (VIII), and Sakellarios[48] failed to obtain the corresponding arsinic acid by cyclization of *o*-carboxydiphenylarsinic acid (IX).



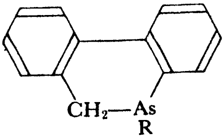
(IX)

Arsanthridines

The name arsanthridine is suggested for the unknown compound (I), which corresponds to phenanthridine with the nitrogen atom replaced by arsenic, and which is isomeric with arsacridine. Derivatives of constitution (II) will almost certainly prove less difficult to synthesize than those of the parent arsanthridine, even assuming that stability factors allow this compound to exist; these derivatives of type (II) are systematically named 10-substituted 9,10-dihydroarsanthridines. If the name arsanthridine is not adopted, then compounds of type (II) must be termed 9-substituted 9,10-dihydro-9-arsaphenanthrenes.



(I)



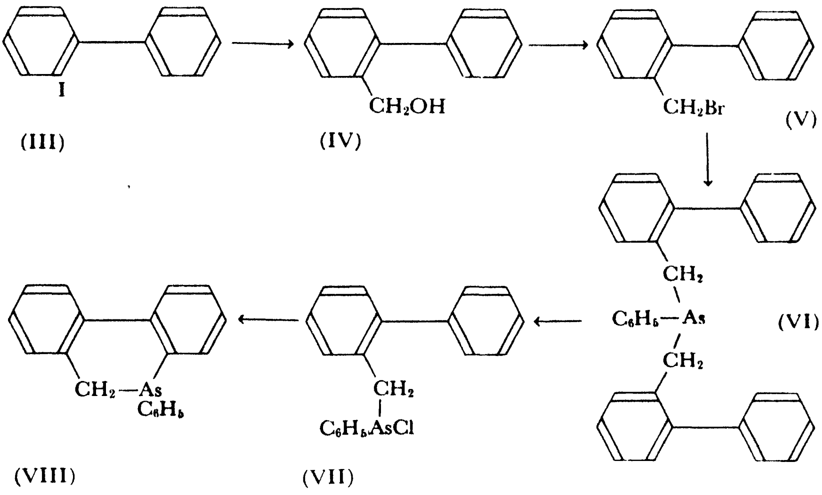
(II)

The following syntheses of compounds of type (II) by Cookson and Mann,[49] clearly establishes the existence of such compounds. In this synthesis, 2-iodobiphenyl (III) was converted into a Grignard reagent, which when treated with formaldehyde yielded 2-biphenylylmeth-

---

[48] Sakellarios, *Ber.*, **59**, 2552 (1926).

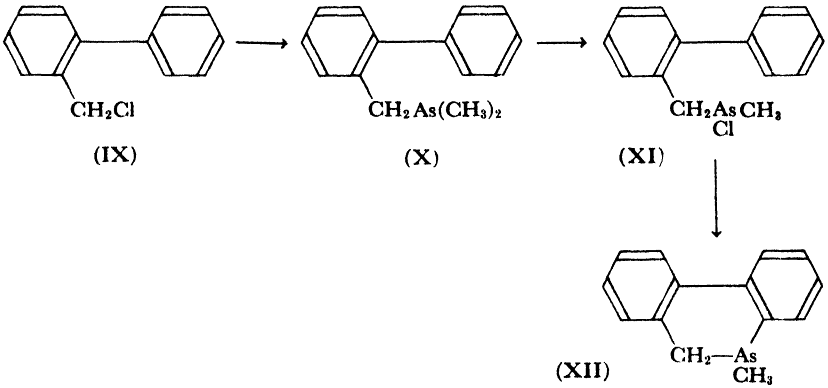
[49] G. H. Cookson and Mann, *J. Chem. Soc.*, **1949**, 2888.



anol (IV), in turn converted to 2-biphenylylmethyl bromide (V). When this bromide was treated with the di-Grignard reagent prepared from phenylarsine, $C_6H_5AsH_2$, *i.e.*, with $C_6H_5As(MgBr)_2$, it formed bis(2-biphenylylmethyl)phenylarsine (VI), m.p. 80–83°, in high yield. The tertiary arsine (VI) readily combined with one molecular equivalent of chlorine to give the arsine dichloride, whch on heating in a vacuum underwent disruption with loss of one biphenylylmethyl radical and with the formation of (2-biphenylylmethyl)phenylchloroarsine (VII) in low yield. This compound in turn underwent cyclization when heated in carbon disulfide solution with aluminum chloride to form 10-phenyl-9,10-dihydroarsanthridine (VIII). The final yield of this compound was small, however, so that for effective characterization as a pure derivative it was converted into the corresponding dichlorobis(10-phenyl-9,10-dihydroarsanthridine)palladium, $[(C_{19}H_{15}As)_2PdCl_2]$, yellow crystals from dioxane, m.p. 244–245° (decomp.) and the analogous dibromopalladium compound of identical melting point.

It was also converted to the quaternary methiodide, *i.e.*, to 10-methyl-10-phenyl-9,10-dihydroarsanthridinium iodide, cream-colored crystals, m.p. 195°, and to the corresponding picrate, yellow crystals, m.p. 150–151°.

10-Methyl-9,10-dihydroarsanthridine (XII) was obtained by an analogous but simpler route. 2-Biphenylylmethyl chloride (IX) was converted into a Grignard reagent, which reacted readily with dimethyliodoarsine, $(CH_3)_2AsI$, to give the liquid dimethyl-*o*-phenylbenzylarsine (X). This arsine combined with one molecular equivalent of chlorine



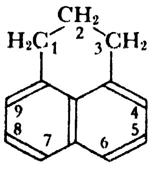
to give the arsine dichloride, which on heating under reduced pressure lost methyl chloride to form methyl-*o*-phenylbenzylchloroarsine (XI). The latter, when heated with aluminum chloride in carbon disulfide solution, underwent ready cyclization to form 10-methyl-9,10-dihydroarsanthridine (XII), which was characterized as the methiodide, *i.e.*, 10,10-dimethyl-9,10-dihydroarsanthridinium iodide, colorless crystals, m. p. 212–215 °.

Cookson and Mann have pointed out that a scale diagram of the 9,10-dihydroarsanthridine ring system (II) shows that, in order to accommodate the central heterocyclic ring, the two *o*-phenylene rings cannot be coplanar; the calculated angle subtended between these two rings, to provide a strainless system, is 34 °. If this twisted structure is rigid, *i.e.*, if there is no oscillation about the axis of the two *o*-phenylene rings, a compound such as the 10-phenyl derivative (VIII) will possess molecular dissymmetry. Furthermore, the quaternary methiodide of the derivative (VIII), which has two unlike groups linked to the arsenic, will in addition have an asymmetric arsenic atom, and consequently should exist in two racemic forms. The actual methiodide of the 10-phenyl derivative isolated by these workers (see above) was, however, a well-defined and apparently homogeneous substance, and no indication of the existence of two racemic forms has yet been detected.

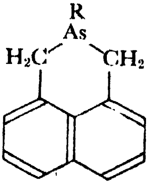
It is noteworthy that the absorption spectrum of biphenyl shows a characteristic absorption band at 252 mμ ($\epsilon_{max.}$ 17,000) which is attributed to the excited states arising from ionic structures of biphenyl in all of which the two benzene rings are linked by double bonds and are hence coplanar. 10,10-Dimethyl-9,10-dihydroarsanthridinium iodide and its 10-methyl-10-phenyl analog have closely similar spectra (see Fig. 1, A), the former having a marked band at 268 mμ ($\epsilon_{max.}$ 11,000) and the latter at 269 mμ ($\epsilon_{max.}$ 9,600). It is probable that these bands are the biphenyl absorption band slightly displaced and reduced in intensity. If so, they indicate that the twisted rings of the biphenyl portion of the dihydroarsanthridine molecule do undergo some oscillation about the coplanar position. Decisive evidence of this point is still lacking however.

2-Arsaperinaphthanes (or 2-Arsaperinaphthindanes)

These compounds are named after the hydrocarbon perinaphthane (I) (*Ring Index* 2031), and hence are termed 2-arsaperinaphthanes (II); it should be noted, however, that the hydrocarbon (I) is sometimes termed perinaphthindane, and, if this term becomes generally adopted, compounds of type (II) will be termed 2-arsaperinaphthindanes.



(I)



(II)

The 2-phenylarsaperinaphthane (II, R = C_6H_5) has been prepared by Beeby, Cookson, and Mann[26] by the interaction of 1,8-bis(bromomethyl)-naphthalene and phenylarsinebis(magnesium bromide). The

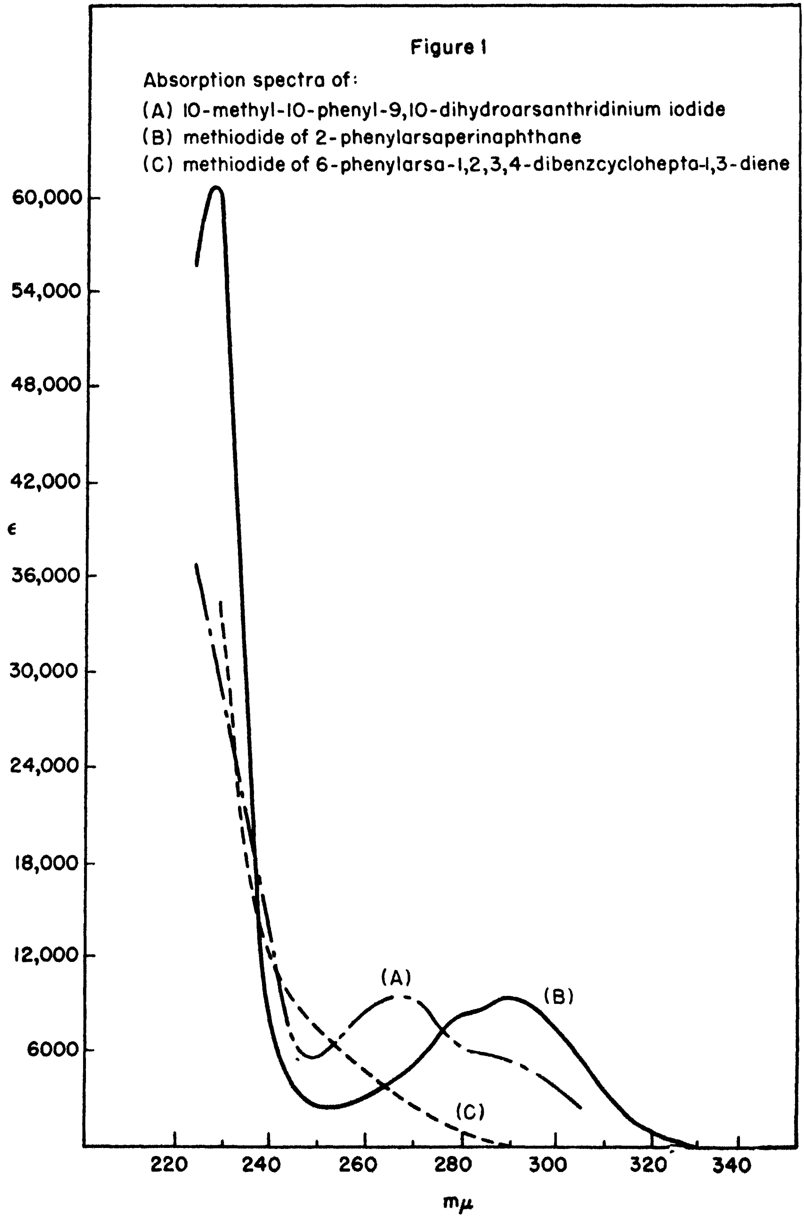


Figure 1

Absorption spectra of:

(A) 10-methyl-10-phenyl-9,10-dihydroarsanthridinium iodide

(B) methiodide of 2-phenylarsaperinaphthane

(C) methiodide of 6-phenylarsa-1,2,3,4-dibenzcyclohepta-1,3-diene tertiary arsine proved very difficult to obtain in the pure crystalline condition, but it readily gave the following crystalline derivatives: quaternary methiodide, colorless crystals, m.p. 196–199°; palladochloride, $[(C_{18}H_{15}As)_2PdCl_2]$, orange microcrystalline powder, which did not melt below 240°.

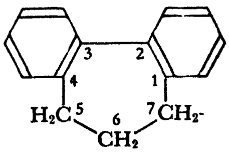
The stability of the above heterocyclic system is shown by the fact that when the phenyl derivative was heated with hydriodic acid of constant boiling point, the phenyl group was replaced by the iodo group, and pale yellow leaflets of 2-iodoarsaperinaphthane (II, R = I), m.p. 117–119°, were obtained. This compound would clearly yield other 2-alkylarsa- and 2-arylarsa derivatives by the action of the appropriate Grignard reagents (*cf.* the isoarsindolines, page 34), and it is consequently a valuable synthetic intermediate.

The ultraviolet absorption spectra of the above quaternary methiodide and of the 2-iodo derivative are almost identical (see Fig. 1, B). In both spectra, the absorption appears to be due mainly to the naphthalene portion of the molecule, but the naphthalene absorption bands are, however, displaced to longer wave lengths by 10–20 mμ. This displacement is of interest because in the above arsanthridinium salts the biphenyl band is also displaced by a comparable amount (16–17 mμ).

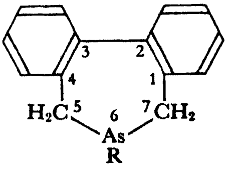
Seven-Membered Ring Systems Containing Only Carbon and Arsenic

6-Arsa-1,2,3,4-dibenzcyclohepta-1,3-dienes

This novel ring system (II) can be regarded as a derivative of the (unknown) hydrocarbon 1,2,3,4-dibenzcyclohepta-1,3-diene (I), in which



(I)



(II)

the methylene group at the 6 position has been replaced by an >AsR group, where R might be an alkyl, aryl, or halogen group. The 6-

phenylarsa derivative (II, R = Ph), has been prepared by Beeby, Mann, and Turner[49a] by the interaction of 2,2′-di(bromomethyl)-biphenyl and phenylarsinebis(magnesium bromide), $C_6H_5As(MgBr)_2$. The arsine readily forms colorless crystals, m.p. 119°, and has the usual properties of a tertiary arsine; *i.e.*, it forms a methiodide, m.p. 224°, and a highly crystalline quaternary *p*-chlorophenacyl bromide. Treatment with hydriodic acid gives the 6-iodo-arsa derivative (II, R = I).

There is little doubt that the tricyclic ring system in compounds of type (II) is not planar, since the two benzene rings are almost certainly twisted at an angle to one another to accommodate the heterocyclic seven-membered ring (*cf.* the arsanthridines, page 54).

Strong evidence on this point is provided by the absorption spectrum (see Fig. 1, C) of the above quaternary methiodide, which shows no absorption band in the 230–300 mμ region, *i.e.*, the characteristic biphenyl absorption band, which requires coplanarity of the benzene rings, is completely absent. It would appear, therefore, that in these compounds the two benzene rings are permanently fixed at an angle to one another, and that in this respect they differ from those in the above arsanthridine derivatives. This aspect of their structure clearly requires further study.

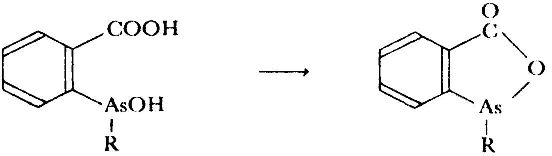
Five-Membered Ring Systems Containing Carbon, Arsenic, and Oxygen

Anhydrides of *o*-Carboxyphenyl Arsinous and Arsinic Acids

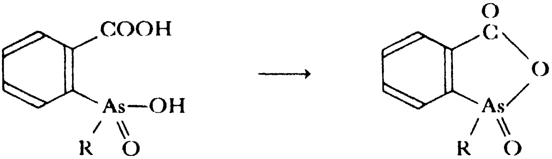
It is clear from the work of Aeschlimann and McCleland[47] that derivatives of *o*-carboxyphenylarsinous acid (I) and arsinic acid (III) can undergo cyclization by loss of water to give the anhydrides (II), R.I. 720, and (IV), respectively, the readiness with which the cyclization proceeds depending largely on the nature of the group R. Alternatively, these anhydrides can be prepared by loss of hydrogen chloride from the corresponding chloro derivatives, in which the As—OH group in (I) and (III) is replaced by the As—Cl group. These anhydrides are therefore closely comparable to the γ-lactones, which can similarly be prepared by loss of water from γ-hydroxycarboxylic acids or by loss of hydrogen chloride from γ-chlorocarboxylic acids.

[49a] Beeby, Mann, and Turner, *unpublished work.*

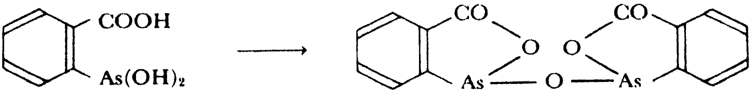
The simplest example of this anhydride formation occurs in the arsonous acid series, in which the phenomenon was first detected by Aeschlimann and McCleland. These workers showed that *o*-carboxyphenylarsonous acid (V) (which they termed benzarsenious oxide hydrate) when heated at 70° in a vacuum lost water with the formation of the anhydride derivative (VI). A more simple example of this cyclization was obtained by heating *o*-carboxyphenyldichloroarsine (VII) at low pressure, when hydrogen chloride was lost with the formation of the chloro anhydride (VIII). This compound formed colorless crystals, m.p. 145°, b.p. *ca.* 220°/15 mm., and when treated in benzene with hydrogen chloride was converted back to the dichloroarsine (VII).



(I) (II)

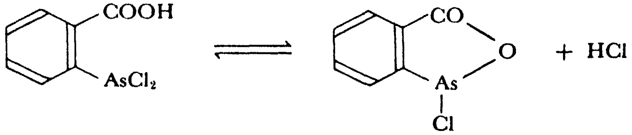


(III) (IV)

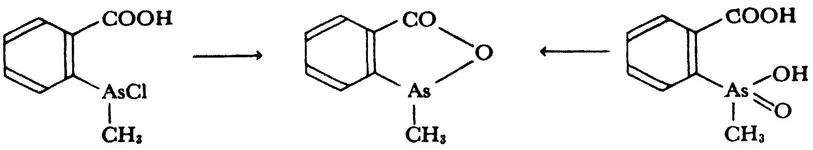


(V) (VI)

The latter method of anhydride formation can also be applied readily to the corresponding arsinous acids. Thus, when *o*-carboxyphenylmethylchloroarsine (IX), a crystalline compound of m.p. 141°, is heated in a vacuum it loses hydrogen chloride with the formation of the methyl anhydride (X), m.p. 106°; this change can also be readily reversed by the action of hydrogen chloride dissolved in benzene. The anhydride (X), however, can also be prepared from *o*-carboxyphenylmethylarsinic acid (XI), which on reduction even in aqueous solution gives the anhydride (X).

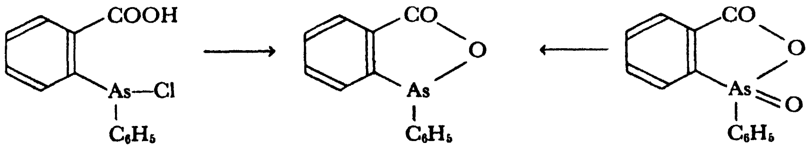


(VII) (VIII)



(IX) (X) (XI)

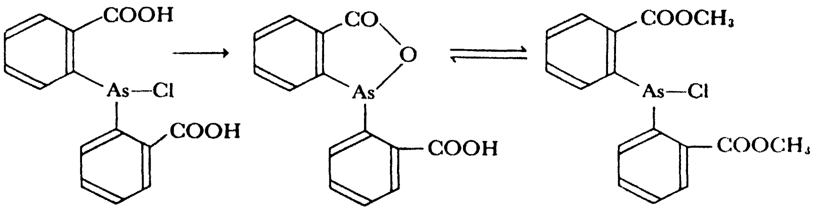
Precisely similar relationships, with one notable exception, hold in the corresponding phenyl series. Thus, *o*-carboxyphenylphenylchloroarsine (XII), of m.p. 163°, when heated in a vacuum gives the phenyl anhydride



(XII) (XIII) (XIV)

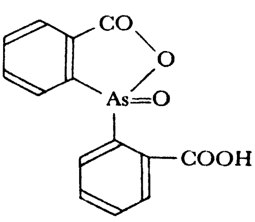
(XIII) of m.p. 133°, a change that can be reversed as before. In this series, however, the *o*-carboxyphenylphenylarsinic acid is apparently unknown, since it passes spontaneously over to the oxy-anhydride (XIV); the latter in turn can be readily reduced to the anhydride (XIII).

This spontaneous formation of the anhydride ring shown in the above *o*-carboxyphenylphenyl compound (XIV) occurs even more readily in the di-*o*-carboxyphenylarsine series of compounds. For instance, di-*o*-carboxy phenylchloroarsine (XV) is unknown, since it passes spontaneously to the carboxyphenyl anhydride (XVI), m.p. 251–255°. When the latter is boiled with methanolic hydrogen chloride, the anhydride ring opens on esterification, with the formation of di-*o*-carbmethoxyphenylchloroarsine (XVII), a crystalline compound of m.p. 184°. When this dimethyl ester is hydrolyzed either with ethanolic potassium hydroxide or even with boiling aqueous hydriodic acid (under the conditions of a Zeisel demethylation), the anhydride (XVI) is again obtained.



(XV) (XVI) (XVII)

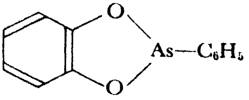
As would be expected from the above reactions, di-*o*-carboxyphenylarsinic acid is unknown, since it also undergoes spontaneous conversion to the anhydride (XVIII). The anhydride ring in this compound has considerable stability and is opened only slowly by cold aqueous alkalis; consequently, the compound acts as a monobasic acid if it is rapidly titrated with a standard alkali solution.



(XVIII)

o-Phenylenephenylarsonite

This compound (I), R.I. 673, can be regarded systematically as a cyclic ester of pyrocatechol and phenylarsonous acid, $C_6H_5As(OH)_2$. Michaelis[50] has shown that when the lead salt of pyrocatechol, of composition $C_6H_4(O)_2Pb$, and phenyldichloroarsine, $C_6H_5AsCl_2$. are mixed in xylene even at room temperature, interaction readily ensues with heat evolution, and the *o*-phenylenephenylarsonite is formed as white crystals, m.p. 83°, b.p. 197–198°/15 mm. The compound reacts readily with water to form pyrocatechol and arsenosobenzene, C_6H_5AsO. This ready hydrolysis recalls the similar hydrolysis of the *o*-phenylenephosphonites (p. 17).



(I)

Spirocyclic Esters of Glycols, *o*-Dihydroxybenzenes, and α-Hydroxycarboxylic Acids with Arsonic Acids

It has been claimed by Salmi, Merivuori, and Laaksonen[51] that alkyl and aryl arsonic acids (I) will condense with 1,2-glycols (II) to give spirocyclic esters of type (III), R.I. 576, and that the condensation proceeds similarly with *o*-dihydroxybenzenes and with α-hydroxycarboxylic acids to give similar spirocyclic derivatives of type (IV), R.I. 2248, and (V). One special example of a α-hydroxycarboxylic acid is cyclohexanol-1-carboxylic acid, which gives compounds of type (VI), similar of course to those of type (V), but with the R_1 and R_2 groups of (V) now forming part of a ring. The esterification can be carried out with the simpler compounds by azeotropic distillation of the components in benzene or toluene, or, if the arsonic acids are insoluble in benzene, by boiling the components with acetic anhydride. Examples of the products obtained are given in Table IV.

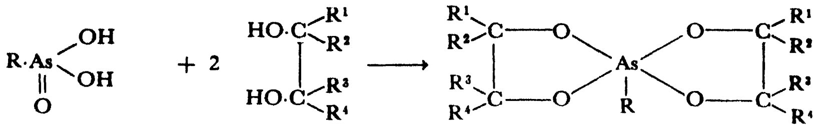
It should be noted that compounds of type (IV) had been recorded earlier by Englund,[52] who found that pyrocatechol in aqueous solution

---

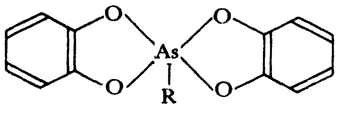
[50] Michaelis, *Ann.*, **320,** 290 (1902).

[51] Salmi, Merivuori, and Laaksonen, *Suomen Kemistilehti*, **B19**, 102 (1946).

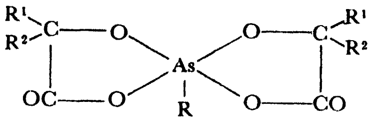
[52] Englund, *Ber.*, **59,** 2669 (1926).



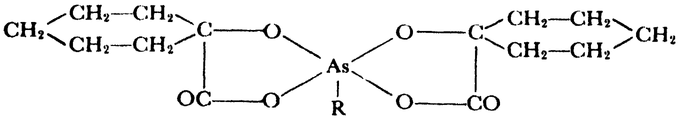
(I) (II) (III)



(IV)



(V)



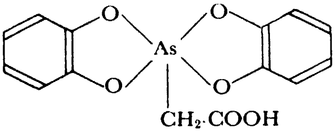
(VI)

TABLE IV[a]

Type	R	R¹	R²	R³	R⁴	M.p., ° C.	B.p., ° C./mm.
(III)	CH_3	H	H	H	H	—	110–111/4
	CH_3	CH_3	H	H	H	—	115.5–116/3
	CH_3	CH_3	CH_3	CH_3	CH_3	—	131–132/3
	n-C_4H_9	H	H	H	H	—	140.5–141.5/3
	n-C_4H_9	CH_3	H	H	H	—	142.6–143.4/5
	n-C_4H_9	CH_3	CH_3	CH_3	CH_3	—	169.0–170/4
	C_6H_5	H	H	H	H	105.5	
	C_6H_5	CH_3	CH_3	CH_3	CH_3	176.0	
(IV)	CH_3	—	—	—	—	151.6	
	n-C_4H_9	—	—	—	—	83.0	
	$C_6H_5CH_2$	—	—	—	—	147	
(V)	C_6H_5	CH_3	CH_3	—	—	138.2	
	C_6H_5	CH_3	C_2H_5	—	—	91.4	
	$C_6H_5CH_2$	CH_3	CH_3	—	—	169	
	$C_6H_5.CH_2$	CH_3	C_2H_5	—	—	161	
(VI)	CH_3	—	—	—	—	213.2	
	n-C_4H_8	—	—	—	—	194	
	$C_6H_5.CH_2$	—	—	—	—	175	

[a] Most of the above solid compounds form canary-yellow crystals.

would not react with arsinoacetic acid or carboxymethylarsonic acid, $HOOC{\cdot}CH_2{\cdot}AsO(OH)_2$, but when the two compounds were boiled together in acetic acid for a short time the product on cooling gave feebly green or blue colored crystals, m.p. 146°, which were considered to be the acid (VII) with one molecule of acetic acid of crystallization. The color



(VII)

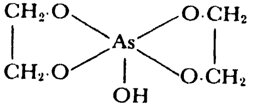
of these crystals was attributed to traces of oxidized pyrocatechol. When the methyl ester of the arsonic acid, *i.e.*, $CH_3OOC{\cdot}CH_2{\cdot}AsO(OH)_2$, was used in the above preparation, the methyl ester of the acid (VII) was obtained as canary-yellow crystals, which were free from solvent of crystallization and were stable in air. It should be remarked, however, that the identification of these compounds rests solely on arsenic analyses carried out on the acid (VII) and its ester, and on an estimation of the acetic acid of crystallization based on the loss in weight of the above crystals, m.p. 146 °, when heated.

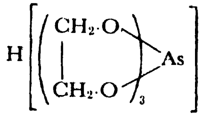
Englund[53] had also briefly recorded the preparation of some compounds similar to those of type (III), except that a hydroxyl group was linked to the arsenic atom in place of the alkyl or aryl group shown in (III). This difference appears to affect markedly their stability, in particular to hydrolysis. For example, Englund states that arsenic acid, H_3AsO_4, dissolves in ethylene glycol on gentle warming, and that on cooling the solution deposits large colorless crystals of the diethylenedioxyarsenic acid (VIII). This acid can be recrystallized from ethanol and then has m.p. 120°. It is stable in air, but is immediately hydrolyzed in water, and, consequently, when titrated with alkalis acts merely as a solution of arsenic acid. In bromoform solution it shows a molecular weight twice that required by formula (VIII), but this result is presumably due to association in solution—although it should be remarked that bromoform very rarely acts as an associating solvent. The crystalline but deliquescent pyridine salt and also the brucine salt of the acid (VIII) are described.

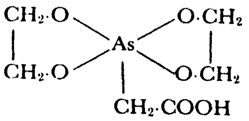
---

[53] Englund, *J. prakt. Chem.*, **120**, 179 (1929).

Englund states that, if arsenic acid is dissolved in three molecular equivalents of ethylene glycol by warming, the product deposits a mixture of the acid (VIII) and tri(ethylenedioxy)arsenic acid (IX) on cooling, the latter apparently analogous in type to the tripyrocatechylarsenic acid described later (p. 67). Recrystallization from various solvents failed to furnish the pure acid (IX), but the aniline, pyridine, and brucine salts are described. However, these three salts were identified solely by their arsenic content.

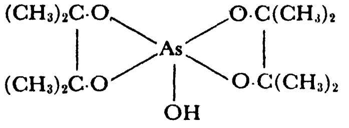

(VIII)

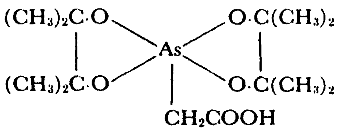

(IX)


(X)

When arsinoacetic acid, HOOC·CH$_2$·AsO(OH)$_2$, is added to a methanol solution of ethylene glycol, complete dissolution occurs on gentle warming, and the product, when cooled and stirred, deposits the crystalline acid (X) m.p. 142 °, which is bimolecular in bromoform solution. This compound is also immediately hydrolyzed by water.

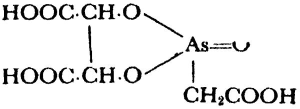
Pinacol appears to form similar compounds even more readily than ethylene glycol, and the products have rather greater stability. For example, if arsenic acid and pinacol are dissolved in acetone, and the solvent then allowed to evaporate spontaneously, long crystals of the acid (XI) are deposited: these can be recrystallized from acetone and then have m.p. 131 °. Englund states that this acid will dissolve in ice-cold water without hydrolysis, and can be titrated as such with dilute alkalis using phenolphthalein as an indicator. At room temperature the aqueous solution soon undergoes hydrolysis.


(XI)


(XII)

Arsinoacetic acid similarly reacts with pinacol in ethanolic solution to give the acid (XII), m.p. 188°. This compound, however, is hydrolyzed rapidly by water.

Arsinoacetic acid also reacts rapidly with *d*-tartaric acid in boiling acetic acid solution to form the crystalline monocyclic acid (XIII). It is significant that *meso*-tartaric acid would not form a similar compound, the configuration of the two asymmetric carbon atoms in this case apparently inhibiting the formation of the ring system.



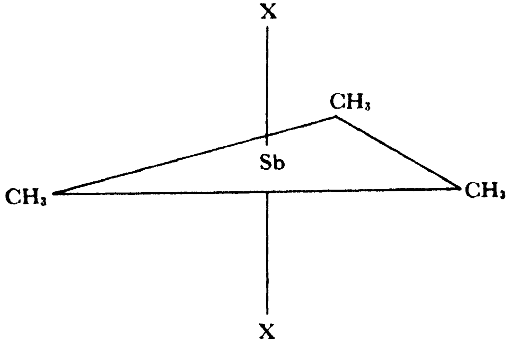
(XIII)

The above compounds are of very considerable interest because in each compound the arsenic atom is apparently 5-covalent. This is an unusual valency state for arsenic, although it appears to be present in the tertiary arsine dichlorides of formula R_3AsCl_2 and in the dihydroxides, $R_3As(OH)_2$, which many of these dichlorides give on complete hydrolysis. Now the dichlorides might be formally represented as ionic compounds of type $[R_3\overset{+}{As}Cl]\overset{-}{Cl}$. It is noteworthy, however, that x-ray analysis[54] of the analogous trimethylstibine dihalides, $(CH_3)_3SbX_2$ (where X represents Cl, Br, or I) has shown that in these compounds the antimony lies in the center of an equilateral triangle whose apices are occupied by the methyl groups, and that the halogen atoms lie on an axis running through the antimony atom at right angles to the triangle (XIV). The important point, however, is that in the dibromide, for example, the two Sb-Br distances are identical and are intermediate between that required for a covalent and for an electrovalent bond, *i.e.*, the bond is a resonance hybrid between the two types of link. It is highly probable, therefore, that, in the tertiary arsine dichlorides, each As—Cl bond is a resonance hybrid having 50% covalent and 50% electrovalent character, and that in these compounds the arsenic can still be accurately regarded as 4-

---

[54] Wells, Z. *Krist.*, **99**, 367 (1938).

covalent. The same reasoning clearly applies to the tertiary arsine dihydroxides. It should be noted, however, that even if the tertiary arsine dichlorides have a resonance structure, they do apparently revert to the ionic form $[R_3\overset{+}{A}sCl]\overset{-}{Cl}$ when undergoing certain reactions. Thus, many tertiary arsine and phosphine dichlorides and dibromides[55] are readily hydrolyzed to the hydroxy chloride, but the hydrolysis of the second chloro group may require the action of hot aqueous alkalis.



(XIV)

It could be similarly suggested that in the compounds (III), (IV), (V), (VI), and (VII), for example, each As—O link is a resonance hybrid bond having 75% covalent and 25% electrovalent character. However, there is no decisive evidence at present for the nature of these bonds.

Tripyrocatechylarsenic Acid

Two different types of arsenic derivative of pyrocatechol have been described above; the compound now being discussed, tripyrocatechylarsenic acid, represents a third and entirely different type.

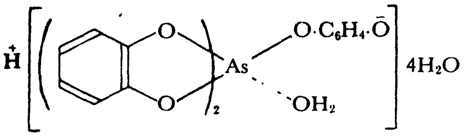
Weinland and Heinzler[56] showed that if pyrocatechol was added to a boiling aqueous solution of arsenic acid, H_3AsO_4, and the solution then filtered and set aside, colorless crystals separated to which they gave the structure (I). It was noteworthy that the same compound was obtained if the molecular ratio of pyrocatechol to arsenic acid was 1:1, 2:1, 3:1, or 1 : 2. With regard to this structure, the following points should be noted. (*a*) The structure ignores the strong tendency of pyrocatechol to form cyclic or chelated rings, of which several examples have already been given. (*b*) Although Weinland and Heinzler prepared a number of simple salts of the acid, the compound was acting as a monobasic acid in the formation of all these salts, and never as a tribasic acid.

---

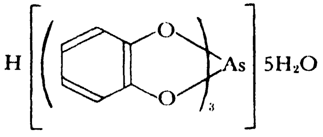
[55] Mann and Chaplin, *J. Chem. Soc.*, **1937**, 527.
[56] Weinland and Heinzler, *Ber.*, **52**, 1316 (1919)

$$\overset{+}{H}_3[\cdot O\cdot As—(O\cdot C_6H_4\cdot \bar{O})_3]4H_2O$$

(I)



(II)



(III)

Reihlen, Sapper, and Kall[57] drew attention to the monobasicity of this acid, but also pointed out that only four molecules of water could be detached from the acid, the elements of the fifth molecule remaining tenaciously in the acid and its salts. Consequently, they allotted the structure (II) to the acid. In this structure the acid is monobasic, two molecules of catechol are chelated to the arsenic, but the third is linked by only one bond, and the one molecule of water is coordinated to the arsenic atom, which is thus showing a coordination number of six. They also demonstrated that a similar stable acid (and salts) could be obtained in which the coordinated molecule of water was replaced by a molecule of pyridine—also firmly attached.

Rosenheim and Plato[58] considered that all three pyrocatechol residues were chelated to the 6-coordinated arsenic atom, and that the compound was consequently tripyrocatechylarsenic acid pentahydrate of structure (III); they admitted, however, that only four of the molecules of water of crystallization could be readily removed, the fifth being firmly linked. If the acid has the structure (III), it should be resolvable into optically active forms because it is of the same general stereochemical type as, for example, potassium cobaltioxalate. They were able, therefore, to resolve the acid through its cinchonine salt, which furnished the *levo*rotatory acid, and through the cinchonidine and quinine salts, which furnished the *dextro*rotatory acid.

---

[57] Reihlen, Sapper, and Kall, *Z. anorg. Chem.*, **144,** 218 (1925).

[58] Rosenheim and Plato, *Ber.*, **58,** 2000 (1925).

Table V gives the composition and rotation of some of the compounds isolated by Rosenheim and Plato. The optically active anion undergoes only slow racemization in neutral aqueous solution and has a surprising optical stability in the presence of caustic alkalis, a short boiling with aqueous sodium hydroxide leaving the rotation almost unchanged. The anion is very sensitive to acids, however, which causes immediate racemization; this would be expected because acids would certainly readily break the chelated pyrocatechol ring.

TABLE V

Salt	Rotation[a]	Solvent
	Dextro Series	
$H[As(C_6H_4O_2)_3]5H_2O$	+2002.6°	Aqueous acetone
$K[As(C_6H_4O_2)_3]1H_2O$	+2218.0°	Aqueous acetone
	Levo Series	
$H[As(C_6H_4O_2)_3]5H_2O$	−2187.5°	Aqueous acetone
$K[As(C_6H_4O_2)_3]1H_2O$	−2097.1°	Aqueous acetone
$NH_4[As(C_6H_4O_2)_3]1H_2O$	−2483.4°	Aqueous acetone
$\frac{Ba}{2}[As(C_6H_4O_2)_3]5H_2O$	−2325.5°	Water

[a] The rotations are cited as given by the authors, although five significant figures are clearly not warranted by their measured rotations.

The structure of the acid still remains uncertain in one respect, however. It is to be noted that all the salts isolated by Rosenheim and Plato—salts of metals, ammonia, and alkaloids—contained at least one molecule of water. Furthermore the structure (II) put forward by Reihlen, Sapper, and Kall would also allow optical activity if the unchelated pyrocatechyl group and the molecule of water occupied the *cis* or 1,2-positions in the 6-coordination octahedron.

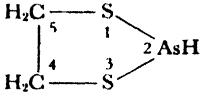
The optically active tripyrocatechylarsenic acid has been employed by Mann and Watson[59] in an unsuccessful attempt to resolve a dissymmetric tetra-aryl arsonium salt. The salt thus investigated, *p*-bromophenyl-*p*-chlorophenyl-phenyl-4-*o*-xylylarsonium *l*-tripyrocatechylarsenate, is the only anhydrous salt which has been recorded. However, this salt has so great a molecular weight that the addition of one molecule of water would hardly affect the carbon and hydrogen content by which the salt was identified.

The role of this one molecule of water in the acid and its salts therefore still awaits elucidation.

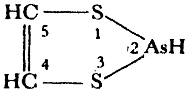
Five-Membered Ring Systems Containing Carbon, Arsenic, and Sulfur

2-Arsa-1,3-dithiacyclopentanes

Compounds of this class can be regarded as derivatives of the unknown arsine (I), R.I. 55, in which the hydrogen atom attached to the arsenic is invariably replaced by other groups. The nomenclature used for these compounds has varied considerably. Cohen, King, and Strangeways,[60] who first isolated compounds of this type, called them "cycloethylenethioarsinites." On the basis of Clark's analogous antimony compounds[61] (p. 150), they might be termed "cyclo-2,5-dithia-3,4-dimethylenearsines." Ruggeberg, Ginsburg, and Cook[62] regarded them as hydrogenated derivatives of the unknown compound (II), and in compliance with *The Ring Index* termed them "4,5-dihydro-1,3,2-dithiarsenoles." Peters and Stocken[63] considered them as cyclopentanes with methylene groups re-



(I)



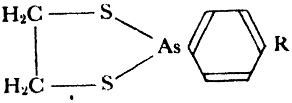
(II)

---

[59] Mann and Watson, *J. Chem. Soc.*, **1947**, 505.
[60] Cohen, King, and Strangeways, *J. Chem. Soc.*, **1931**, 3056.
[61] Clark, *J. Chem. Soc.*, **1932**, 1826.
[62] Ruggeberg, Ginsburg, and Cook, *J. Am. Chem. Soc.*, **68**, 1860 (1946).
[63] Peters and Stocken, *Biochem. J.*, **41**, 53 (1947).

placed by sulfur atoms and by the >AsH group, and called them "1,3-dithia-2-arsacyclopentanes," retaining the numbering suggested by *The Ring Index*. This would appear to be the most satisfactory method of naming, with the prefixes rearranged in alphabetical order. For various reasons, however, it would be preferable to number the arsenic atom 1 and regard it as the key atom in the ring; the numbering given in (I) is retained (rather reluctantly by the present author) in order to reduce to a minimum the sum of the numbers of the fixed substituents in the ring.

Cohen, King, and Strangeways[60] showed that if a mixture of 1,2-ethanedithiol and *p*-acetamidophenyl arsenoxide were boiled in ethanol for ten minutes and cooled, 2(*p*-acetamidophenylarsa)-1,3-dithiacyclopentane (III, R = $CH_3CONH\cdot$) crystallized as colorless leaflets, m.p. 155°. It was soluble in most of the common organic solvents and dissolved unchanged in glacial acetic acid; however, it was readily decomposed by both alkalis and the mineral acids. The corresponding *p*-carboxy derivative (III, R = $HOOC\cdot$) was similarly prepared as colorless crystals, m.p. 223–224°.



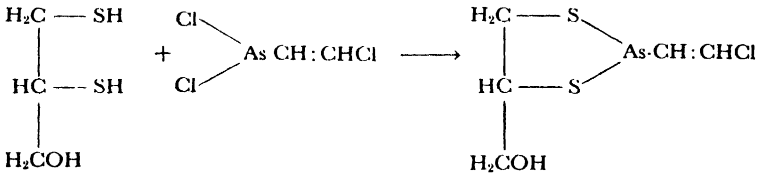
(III)

Considerable impetus was given to the study of compounds having the ring structure (I) by the discovery by Peters in the early stages of World War II that certain 1,2-dithiols, but especially 2,3-dithiolpropanol (III), would condense readily with dichloroarsines, and thus provided an effective treatment for contamination in particular by primary lewisite, $Cl_2As(CH{:}CHCl)$. A great deal of work on the chemical and physiological aspects of this subject has been done by British and American workers both during and since the war, and much of this is almost certainly still unpublished. Peters, Stocken, and Thompson,[64] giving a brief account of the basis of this work after the security regulations had been partly lifted, pointed out that 2,3-dithiolpropanol (III)—termed BAL (British

---

[64] Peters, Stocken, and Thompson, *Nature*, **156**, 611 (1945).

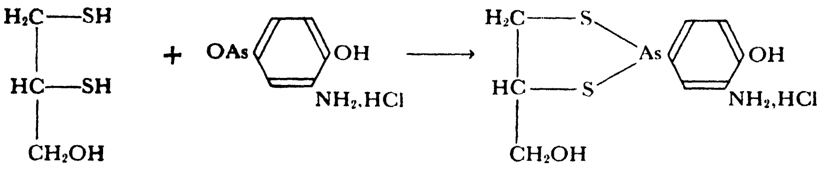
Anti-Lewisite) by the American workers—reacted with primary lewisite (IV) to give the cyclic derivative (V), *i.e.*, 4-hydroxymethyl-2-(2-chlorovinylarsa)-1,3-dithiacyclopentane (V). They state that various 1,2- and 1,3-dithiols were condensed with dichloroarsines to give compounds of type



(III) (IV) (V)

(V) and (presumably) the corresponding cyclohexane derivatives, but that BAL, in particular, "proved highly effective in stopping the toxic action of lewisite upon the pyruvate oxidase system in brain."

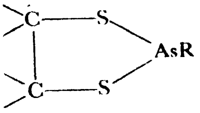
A further example of cyclization by BAL was given later by Peters and Stocken,[63] who showed that if an ethanolic solution of the drug matharside—or 3-amino-4-hydroxyphenylarsenoxide hydrochloride (VI)—containing an equivalent quantity of BAL were evaporated in a vacuum desiccator, crystals of the hydrochloride of 4-hydroxymethyl-2(3′-amino-4′-hydroxyphenylarsa)-1,3-dithiacyclopentane (VII), m.p. 172–173°, were obtained.



(III) (VI) (VII)

The two methods of synthesizing the ring system (I), namely by the condensation of a 1,2-dithiol with a dichloroarsine or an arsenoxide, are thus illustrated.

An excellent account of the chemistry, biochemical action, toxicology, pharmacology, and medical applications of 1,2-dithiols such as BAL has been given by Waters and Stock.[65] This account contains too much material to be summarized here. It should be noted, however, that the authors state that the available evidence indicates "that dithiols added to protein previously treated with arsenic probably compete successfully for the arsenic by formation of compounds of type (VIII)." And furthermore, that this evidence focused "attention on the theory that the toxicity of trivalent arsenicals is largely due to their binding of essential thiol groups in enzyme proteins." The very great biological importance of the heterocyclic system shown in (VIII) is thus manifest.



(VIII)

It should be noted that the therapeutic properties of the hydrochloride (VII) obtained by the condensation of BAL and matharside (the latter compound being sometimes termed mapharsen), and of the base corresponding to the hydrochloride (VII), have been investigated by Friedheim and Vogel.[65a] They find that both the base and the hydrochloride are stable compounds, and indeed that solutions of the hydrochloride in propylene glycol can be sterilized by heating for one hour at 100 °. The base was found to possess spirochetocidal action when tested against rabbit syphilis, and the hydrochloride to have trypanocidal action when tested against *T. equiperdum* in mice.

Friedheim and Berman[65b] have shown further that the trichomonacidal action of matharside is significantly increased when it is condensed with BAL to give the compound (VII). On the other hand, condensation of *p*-3-carboxypropylphenylarsenoxide (or γ-*p*-arsenophenylbutyric acid), $O{:}As.C_6H_4.CH_2CH_2CH_2.COOH$, with BAL to give 4-hydroxymethyl-2(*p*-3-carboxypropylphenylarsa)-1,3-dithiacyclopentane (IX) was not accompanied by the development of any significant trichomonacidal action. These workers suggest that this is probably because "the strongly polar anionic character of the butyric acid residue precludes the degree of lipid solubility necessary for a trichomonacidal effect."

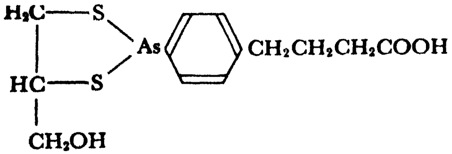
---

[65] Waters and Stock, *Science*, **102**, 601 (1945).

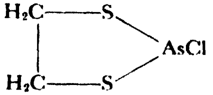
[65a] Friedheim and Vogel, *Proc. Soc. Exptl. Biol. Med.*, **64**, 418 (1947).

[65b] Friedheim and Berman, *Proc. Soc. Exptl. Biol. Med.*, **65**, 180 (1947).

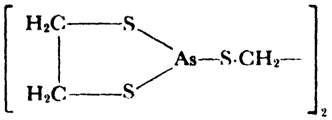
Ruggeberg, Ginsburg, and Cook[62] have utilized this 1,2-dithiol condensation to obtain some very interesting and simple derivatives of the parent compound (I). Thus, when ethanedithiol was added to a solution of arsenic trichloride in carbon tetrachloride, hydrogen chloride was instantly liberated and the endothermic reaction caused a marked fall in the temperature of the solution, since colorless crystals of 2-chloroarsa-1,3-dithiacyclopentane (X), m.p. 37.5–38°, separated. In an attempt to oxidize this compound to the corresponding arsinic acid, the 2-chloro derivative was dissolved in aqueous ethanol and maintained at 80° for 2 hours while air was bubbled through the solution. When recrystallised from benzene, the product had m.p. 82–83°, but analysis indicated that it was the compound (XI). This result probably indicates that some of the 2-chloro compound (X) had undergone hydrolytic fission to arsenious acid and ethanedithiol, and that the latter had then readily condensed with two molecular equivalents of the unhydrolyzed 2-chloro compound to form the dicyclic derivative (XI).



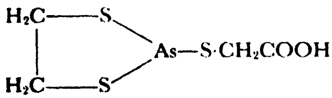
(IX)



(X)



(XI)



(XII)

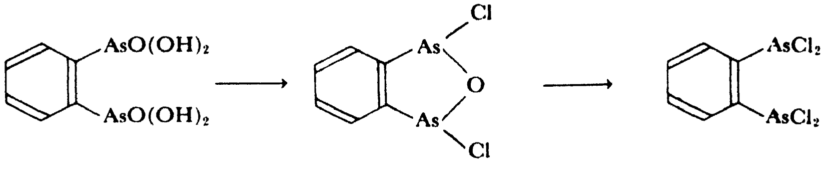
When a benzene solution of the 2-chloro compound (X) containing an equivalent of thioglycollic acid, HS·CH$_2$·COOH, was refluxed for 3 hours until hydrogen chloride evolution was complete, the solution furnished 2-(carboxymethylthioarsa)-1,3-dithiacyclopentane (XII), colorless crystals from benzene, m.p. 77–80°.

In view of the ease with which derivatives of the compound (I) can be synthesized and of the biological importance of certain of the members, there is clearly a wide field of research available here.

Five-Membered Ring Systems Containing Carbon, Oxygen, and Two Arsenic Atoms

Anhydride of *o*-Phenylene-bis(arsonous Chloride)

Kalb[66] has shown that when *o*-phenylenediarsonic acid (I) is reduced by means of sulfur dioxide in concentrated hydrochloric acid solution containing a trace of potassium iodide, the colorless crystalline dichloro anhydride (II), m.p. 148°, is obtained. No molecular weight determinations on this compound have been recorded, but it is highly probable that it contains the five-membered ring structure depicted above.



(I) (II) (III)

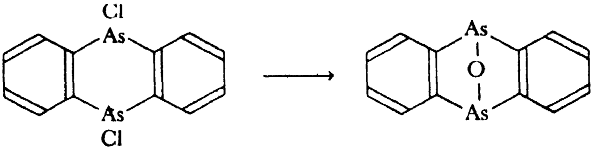
Kalb was unable to convert this anhydride into the *o*-phenylenebis(dichloroarsine) (III), but this conversion was subsequently achieved by Chatt and Mann[67] using thionyl chloride.

Anhydride of 5,10-Dihydroxy-5,10-dihydroarsanthrene

This compound would be more conveniently discussed with other arsanthrene derivatives (p. 119), but for systematic reasons the possible presence of a five-membered ring necessitates brief mention of the compound at this stage. However, it is recommended that the reader first consult p. 117 *et. seq.* for a discussion of the nomenclature and properties of arsanthrene and its derivatives.

---

[66] Kalb, *Ann.*, **423**, 39 (1921).
[67] Chatt and Mann, *J. Chem. Soc.*, **1939**, 610.



(I) (II)

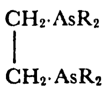
Kalb[66] has shown that when 5,10-dichloro-5,10-dihydroarsanthrene (I), R.I. 1831, is shaken for several hours at room temperature with a mixture of ether and aqueous sodium hydroxide, hydrolysis and cyclization occur to give a compound to which he allotted structure (II) and which he named "arsanthrene oxide." It forms colorless crystals, m.p. 196°, slightly soluble in ethanol and ether, readily soluble in benzene, chloroform, and carbon disulfide.

If the compound has the structure (II), it is the anhydride of 5,10-dihydroxy-5,10-dihydroarsanthrene. However, consideration of the intervalency angles in arsanthrene derivatives shows that although 5,10-disubstituted derivatives may possibly, in certain cases, exist in three forms (*cf.* XIV A, B, and C, p. 122), most such compounds can actually exist only in two of these forms (A and B). If the 5,10-dihydroxy compound possessed either of these configurations, the two hydroxy groups would be too far apart for anhydride formation. Therefore, it follows that the anhydride either has a configuration corresponding to (XIV C, p. 122) or is formed by loss of water from two or more molecules of the 5,10-dihydroxy derivatives reacting together. Its melting point and solubility relationships, however, probably indicate a comparatively simple structure. It is unfortunate that the molecular weight of this compound has not been determined.

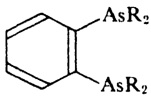
Five-Membered Ring Systems Containing Carbon, Palladium, and Two Arsenic Atoms

The compounds discussed in this section differ in one notable respect from all those in previous sections. In the heterocyclic derivatives of arsenic hitherto discussed, the ring system has consisted of atoms linked together by simple covalent bonds. In the present compounds, cyclization is achieved by the arsenic atoms being coordinated to palladium, producing an exceedingly stable ring formation.

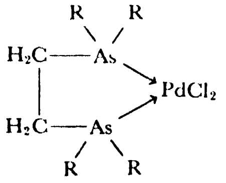
Chatt and Mann[67,68] have prepared certain 1,2-ditertiary arsines, such as ethylene-1,2-bis(dimethylarsine) (I, R = CH_3), and the corresponding bis(di-*n*-butylarsine) (I, R = *n*-C_4H_9) and the bis(diphenylarsine) (I, R = C_6H_5), and also *o*-phenylenebis(dimethylarsine) (II, R = CH_3), and the corresponding bis(di-*n*-butylarsine) (II, R = *n*-C_4H_9). All these ditertiary arsines coordinate under suitable conditions with palladium dichloride to give nonionic derivatives of type (III) or (IV), which are insoluble in water but soluble in most organic solvents. These yellow crystalline compounds usually have sharp melting points: the members in which R is a methyl group, however, usually decompose before melting, but as the group R proceeds up the homologous series of alkyl groups the melting point falls steadily (*cf.* Mann and Purdie[69]) As examples, the compounds in Table VI can be quoted:


$$\begin{array}{l} CH_2{\cdot}AsR_2 \\ | \\ CH_2{\cdot}AsR_2 \end{array}$$

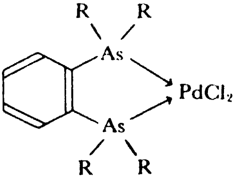
(I)



(II)



(III)



(IV)

---

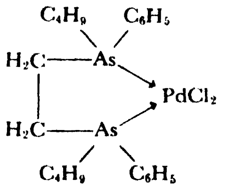
[68] Chatt and Mann, *J. Chem. Soc.*, **1939**, 1622.

[69] Mann and Purdie, *J. Chem. Soc.*, **1935**, 1549.

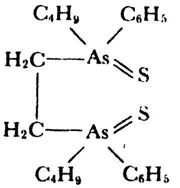
TABLE VI

Compound	M.p.
Ethylene-1,2-bis(di-*n*-butylarsine)dichloropalladium	221°
Ethylene-1,2-bis(diphenylarsine)dichloropalladium	Decomp.
o-Phenylenebis(dimethylarsine)dichloropalladium	300°
o-Phenylenebis(di-*n*-butylarsine)dichloropalladium	273–275°

The chief interest in these compounds is in ethylene-1,2-bis(*n*-butylphenylarsine)dichloropalladium (V). This compound, unlike the previous examples in this class, possesses two asymmetric arsenic atoms, *i.e.*, atoms joined to four unlike groups; moreover, the set of four unlike groups joined to each arsenic atom is identical. Consequently, the compound should theoretically exist in two distinct forms: a *meso* and a *racemic* form. Chatt and Mann[68] were able to separate the crude product into two distinct forms, of which the α form had m.p. 172–174°, and the β form had m.p. 185–186°. A mixture of approximately equal quantities of both forms had m.p. 137–150°. It is not known, of course, which of these forms is the *meso* and which the *racemic* compound. The stability of these isomers is noteworthy: each form could be maintained in the molten condition just above its melting point for 1½ hours without any indication of conversion to the other form. Similarly, each form was unaffected when boiled in ethanol solution for 2 hours. Interconversion, had it occurred, would have involved a change of configuration of one of the arsenic atoms. The ring system in (V) is so stable, however, that the constituent atoms appear to be locked firmly in position, and consequently no change of configuration occurs. This is in marked contrast to the noncyclic disulfide (VI), which Chatt and Mann[67] have also



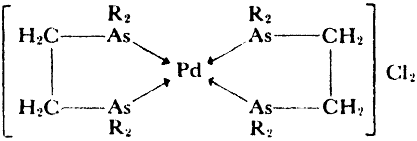
(V)



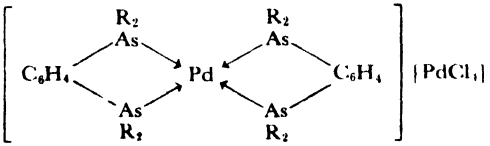
(VI)

separated into two forms, α, m.p. 113–116°, and β, m.p. 120–121°, but in which the α form readily passes over into the β-form.

It is of interest to note that the above cyclic diarsinepalladium compounds are usually prepared by shaking the diarsine with an aqueous-ethanolic solution of ammonium palladochloride, $(NH_4)_2[PdCl_4]$. In certain cases this treatment produces the ionic bisdiarsine palladium dichloride (VII) or its palladochloride (VIII). Conversion to the co-



(VII)



(VIII)

valent monocyclic compound (types III, IV, and V) can usually be effected by boiling compounds of type (VII) with ammonium palladochloride dissolved in aqueous-ethanolic hydrochloric acid, and by boiling compounds of type (VIII) with aqueous ethanolic hydrogen chloride alone. Both types of compound, (VII) and (VIII), contain spirocyclic cations.

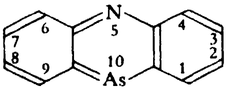
In all the above palladium compounds, the arsenic has been depicted as joined by a coordinate link to the palladium atom. This formulation has been adopted because in these compounds (unlike the tertiary arsine oxides, sulfides, etc.) there is at present no evidence of double bond character.

Since these 1,2-diarsines will coordinate very readily with many of the transitional metals, it is clear that a vast number and variety of these coordinated compounds could be prepared. As an example, it has been shown recently by Allison and Mann[69a] that *o*-phenylenebis(dimethylarsine) readily coordinates with stannic chloride to give tetrachloro-[*o*-phenylenebis(dimethylarsine)]tin, a crystalline compound of composition $[C_6H_4\{As(CH_3)_2\}_2SnCl_4]$ in which the 6-coordinate tin atom is undoubtedly at the center of an octahedron. In this respect it differs from the above palladium compounds, in all of which the 4-coordinate palladium atoms have the planar configuration.

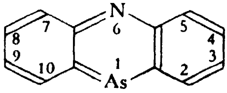
Six-Membered Ring Systems Containing Carbon, Arsenic, and Nitrogen

Phenarsazines

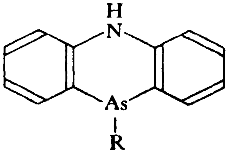
Phenarsazine has the structure (I), R.I. 1827; the numbering shown in (I) is that proposed by Burton and Gibson[70] and adopted in the *Ring Index*; it is used throughout the present work, particularly since it brings the numbering into line with that used in many similar tricyclic systems, *e.g.*, phenoxarsine (p. 100) and arsanthrene (p. 118). It should be noted, however, that the alternative numbering shown in (II) is employed in *Chemical Abstracts*. On the basis of formula (I), it will be seen that the true systematic name for phenarsazine is 5-aza-10-arsa-anthracene; but most derivatives of phenarsazine are of type (III), and are therefore 10-substituted-5,10-dihydrophenarsazines. A considerable number of phenarsazine compounds are known, particularly because cyclization to form the heterocyclic phenarsazine ring system is usually a very simple and ready process. Consequently the present account is not exhaustive: it aims solely at providing a general account of the preparation and properties of phenarsazine derivatives.



(I)



(II)



(III)

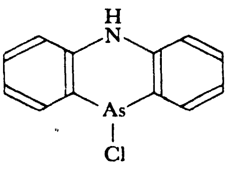
The first announcement of the condensation of diphenylamine and arsenic trichloride to give 10-chloro-5,10-dihydrophenarsazine (IV)

[69a] Allison and Mann, *J. Chem. Soc.*, **1949**, 2915.

[70] Burton and Gibson, *J. Chem. Soc.*, **1926**, 450.

(known as *phenarsazine chloride*) appeared in a patent specification,[71] but the first reasonably full description of the preparation and properties of compounds of this class was provided by Wieland and Rheinheimer.[72] These authors showed that if a mixture of diphenylamine and arsenic trichloride was heated (under reflux) to boiling, hydrogen chloride was evolved and the temperature of the mixture rose to 210° in the course of about 4 hours, when the hydrogen chloride evolution almost ceased. If the hot product was then mixed with boiling xylene, the solution on cooling deposited the crystalline 10-chloro compound (IV), which after recrystallization or sublimation in a vacuum had m.p. 193°. It normally forms pale green needles, which give a yellow powder.

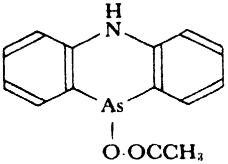
This compound has many of the chemical, and some of the physiological properties of a diaryl monochloroarsine, such as diphenylmonochloroarsine, and without doubt this similarity stimulated much of this earlier research into the phenarsazine series generally. The 10-chloro compound (IV), for example, when in the form of dust or vapor, has an irritating effect on the mucous membrane similar to that of diphenylmonochloroarsine (*cf.* p. 51).



(IV)

$HN:(C_6H_4)_2:As{\cdot}O{\cdot}As:(C_6H_4)_2:NH$

(V)



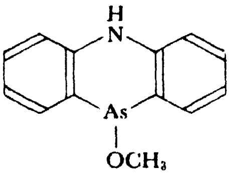
(VI)

On the chemical side, the 10-chloro compound when treated with alkalis gives *phenarsazine oxide*, to which the constitution (V) was allotted. If this constitution is correct, the compound is systematically the anhydride of 10-hydroxy-5,10-dihydrophenarsazine. The compound is very slightly soluble in most solvents and has a melting point "above 350°"; these properties both preclude a molecular weight determination and point to the possibility of a more complex molecule of this composition. When a boiling mixture of the "oxide" and methanol is treated with hydrogen sulfide, the *phenarsazine sulfide*—precisely analogous in formulation to (V)—is obtained as yellow crystals, m.p. 262°. Furthermore, acetic acid readily converts the "oxide" to 10-acetoxy-5,10-dihydrophenarsazine (VI), greenish leaflets, m.p. 223–224°. The much lower melting points of these two compounds and their more ready dissolution in solvents compared with the analogous properties of the "oxide" may have some significance.

---

[71] F. Bayer and Co., German Pat. 281,049 (1915).
[72] Wieland and Rheinheimer, *Ann.*, **423**, 1 (1921).

When the 10-chloro compound (IV) is boiled with sodium methoxide in methanol, the 10-methoxy derivative (VII), colorless needles, m.p. 194°, is formed. A number of such compounds have been prepared.



(VII)

$HN:(C_6H_4)_2.As{\cdot}N:(C_6H_4)_2:As{\cdot}N:(C_6H_4)_2:AsCl$

(VIII)

$[HN:(C_6H_4)_2:As]_3N$

(IX)

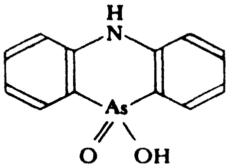
Furthermore, the 10-chloro compound, when heated with silver cyanide, gives the 10-cyano compound, m.p. 227–228 °.[72a]

It will be clear that if the elements of hydrogen chloride could be broken off the 10-chloro compound (IV), the parent phenarsazine (I) would be obtained. Wieland and Rheinheimer showed, however, that when the chloro compound was boiled for two hours with pyridine (or with quinoline or dimethylaniline), a compound termed triphenarsazine chloride, whose composition corresponded with the structure (VIII), was obtained. When the 10-chloro compound in boiling xylene was treated with ammonia gas, triphenarsazine amine (IX) was obtained: this reaction recalls the action of ammonia on molten 2-bromoethylphthalimide, which produces tri(2-phthalimidoethyl) amine, $[C_6H_4(CO)_2N \cdot CH_2CH_2]_3N$.[73]

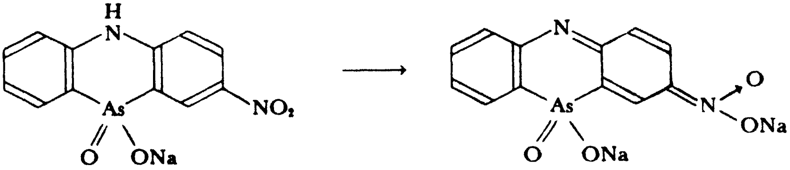
[72a] Grischkievitch-Trochimovski, Matejak, and Zablocki, *Rocz. Chem.*, **7**, 230 (1927).

[73] Ristenpart, *Ber.*, **29**, 2530 (1896).

However, the parent phenarsazine was obtained by heating the 10-methoxy compound (VII) in diphenylmethylamine solution, through which a current of carbon dioxide was passed. In these circumstances, methanol is split off, and the phenarsazine (I) obtained as an orange-yellow product, having a melting point "about 310°." As might be expected, this compound is very reactive. Its solutions become decolorized very rapidly when exposed to air; this effect is apparently caused, not by oxidation, but by absorption of water to give the "oxide" (V). It will also readily combine with alcohols and phenols to give compounds of type (VII), with acetic and other acids to give products of type (VI), and with hydrogen chloride to give the 10-chloro compound (IV). This last addition is apparently the only one which has not been reversed.



(X)



(XI) (XII)

When the 10-chloro compound (IV) is treated in acetic acid solution with hydrogen peroxide, it is converted to phenarsazinic acid (X), colorless needles, m.p. above 300°. Since this acid is clearly an arsinic acid, its name has been changed recently to phenazarsinic acid in *Chemical Abstracts*. The nitro derivatives of this acid are of considerable interest. They can be prepared in two ways. If the 10-chloro compound in acetic acid solution is cautiously treated with fuming nitric acid, the following derivatives can be isolated: 4-nitro, scarlet needles, m.p. 156°; 2-nitro, greenish-yellow leaflets; 2,8-dinitro, pale yellow needles, m.p. $>300°$. If these 10-chloro-nitro derivatives are now treated with hydrogen peroxide in acetic acid, the corresponding nitrophenazarsinic acids are obtained. Alternatively the latter can be obtained by the direct nitration of the phenazarsinic acid (X). The 2-nitrophenazarsinic acid forms two series of salts. For example, it will give a yellow monosodium salt, which is undoubtedly the normal sodium arsinate (XI); with excess sodium hydroxide it will give a cherry-red disodium salt, which is almost certainly a derivative of the *aci* form (XII), in which the right-hand ring necessarily has the quinonoid structure.

These nitro compounds can be reduced by ferrous hydroxide to the corresponding aminophenazarsinic acids, since the arsinic acid group is not affected by this reducing agent. The aminophenazarsinic acids are colorless crystalline compounds having amphoteric properties; the arsinic acid group is not sufficiently strongly acidic to prevent them forming crystalline hydrochlorides, for instance.

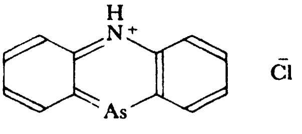
Preparation of 10-chloro-5,10-dihydrophenarsazine, of the oxide (V) and of phenazarsinic acid was described independently by Schmidt[73a] shortly after the appearance of Wieland and Rheinheimer's work.

Burton and Gibson[74] have shown that the oxidation of 10-chloro-5,10-dihydrophenarsazine to the phenazarsinic acid can also be very conveniently carried out by using an aqueous solution of Chloramine-T (sodium *p*-toluene sulfochloroamide, $CH_3{\cdot}C_6H_4SO_2NNaCl{\cdot}3H_2O$), a reaction which appears to be general also for dialkyl and diaryl monochloroarsines, R_2AsCl, which similarly give the corresponding arsinic acids, $R_2AsO(OH)$. These authors also showed that the —NH— group in the 10-chloro compound (IV) could be readily acylated by the action of the appropriate acyl chloride in benzene solution, and that the 10-chloro-5-acyl-5,10-dihydrophenarsazines so obtained could be similarly oxidized by Chloramine-T to the 5-acylphenazarsinic acids. In this way the 5-acetyl, 5-propionyl, and 5-benzoyl derivatives in each series were prepared.

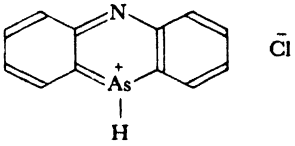
Since 10-chloro-5,10-dihydrophenarsazine is yellow whereas many phenarsazines are colorless, Wieland and Reinheimer[72] considered the possibility of the compound possessing an ammonium structure (IVA), but decided that the majority of its properties were those of a true chloroarsine, and that the structure (IV) is probably correct. Kappelmeier[46] has suggested that the compound is an arsonium salt of structure (IVB).

[73a] Schmidt, *J. Am. Chem. Soc.*, **43**, 2449 (1921).

[74] Burton and Gibson, *J. Chem. Soc.*, **125**, 2277 (1924).



(IVA)



(IVB)

In support of this structure he points out that (*a*) the compound is yellow compared with the colorless diphenylchloroarsine—the structure of which is certain, (*b*) the action of bromine is not to form a bromide or a perbromide, but to split the molecule into tetrabromodiphenylamine and arsenic tribromide, and (*c*) the compound frequently "behaves as the chloride of a weak base." None of these arguments is convincing. That given under (*b*) is of course merely evidence of the instability of the heterocyclic ring toward certain reagents: it will be noted that hydrogen chloride will itself break this ring, reversing the original synthesis and yielding diphenylamine and arsenic trichloride. The balance of evidence remains heavily in favor of structure (IV).

When 10-chloro-5,10-dihydrophenarsazine is reduced in ethanolic acetone solution with hypophosphorous acid, it gives 10,10′-bis-5,10-dihydrophenarsazine, $HN{:}(C_6H_4)_2{:}As.As{:}(C_6H_4)_2{:}NH$, m.p. 304–305°.[75] The same compound is obtained when phenazarsinic acid in acetone solution containing a trace of iodine is similarly reduced with hypophosphorous acid. It is a reasonably stable compound, but in hot xylene solution undergoes ready oxidation back to phenazarsinic acid. It has been suggested that this compound, in view of its orange-yellow color and ready oxidation, might exist partly (or wholly) as free radicals:

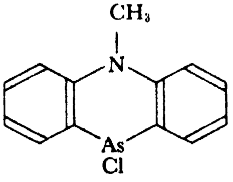
$$HN{:}(C_6H_4)_2{:}As\cdot As{:}(C_6H_4)_2{:}NH \rightleftharpoons 2HN{:}(C_6H_4)_2{:}As\cdot$$

The compound has been found to be diamagnetic, however, and hence the solid material must consist of the dimeric form with no detectable amount of the above free radical.[75a]

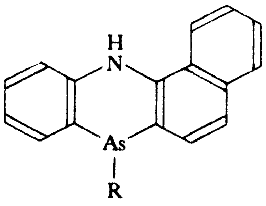
---

[75] Burton and Gibson, *J. Chem. Soc.*, **1926**, 2241.

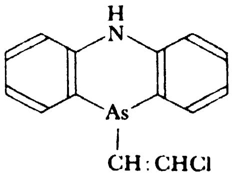
With regard to the preparation of 5- and 10-substituted phenarsazines, it should be noted that Wieland and Rheinheimer[72] claimed that the phenarsazine cyclization was not peculiar to secondary diaryl amines, because they stated that diphenylmethylamine, $(C_6H_5)_2NCH_3$, would similarly condense with arsenic trichloride to give 10-chloro-5-methyl-5,10-dihydrophenarsazine (XIII), yellowish-green needles, m.p. 203°, although the yield was much lower than that of the unmethylated product (IV). Lewis and Hamilton[76] showed that phenyl-1-naphthylamine condensed readily with arsenic trichloride when heated up to 200° in the course of 2 hours to give 3,4-benz-10-chloro-5,10-dihydrophenarsazine (XIV, R = Cl). This compound formed yellow crystals, m.p. 219°, and had only a slightly irritating action on the mucous membrane of the nose and throat. It is interesting to note that when treated with hydrobromic acid this compound gave the 10-bromo compound (XIV, R = Br), dark yellow needles, m.p. 227°, and with hydriodic acid gave the 10-iodo compound (XIV, R = I), red needles, m.p. 205°. A series of 10-alkoxy and other derivatives were also made. Lewis and Stiegler[77] claimed that 2-chlorovinyldichloroarsine, ClCH:CHAsCl₂, in the above condensation gave 3,4-benz-10-(2-chlorovinyl)-5,10-dihydrophenarsazine (XIV, R = CH:CHCl), bright yellow needles, m.p. 213°. For this condensation, the reactants were heated together for only 15 minutes;



(XIII)



(XIV)



(XV)

[75a] Allen and Sugden, *J. Chem. Soc.*, **1936**, 440.
[76] Lewis and Hamilton, *J. Am. Chem. Soc.*, **43**, 2218 (1921).
[77] Lewis and Stiegler, *J. Amer. Chem. Soc.*, **47**, 2546 (1925).

too long heating, too high a temperature, or the use of catalysts produced only a tar, while no reaction occurred in boiling xylene. These workers also claimed that the condensation of diphenylamine with 2-chlorovinyldichloroarsine gave 10-(2-chlorovinyl)-5,10-dihydrophenarsazine (XV), m.p. 186–187°, which had a very irritating action on the eyes and nose. The validity of these claims to have prepared either the 5-methyl derivative (XIII) or the 10-(2-chlorovinyl) derivatives of type (XIV) and (XV) will be discussed later.

In 1926 there appeared the first[70] of a long series of papers [70,76,78–93] by Gibson and his co-workers which have vastly increased our knowledge of the preparation, structure, and properties of phenarsazine derivatives. The interested reader is referred particularly to the first paper,[70] in which (in a footnote) a brief account is given of the various independent centers of research on phenarsazines which were operating during World War I; this account is valuable because it is clear that many of the early discoveries in phenarsazine chemistry were made independently by various workers, and it is now not possible to assert who first prepared (as distinct from recorded in open publication) many of the more simple phenarsazine derivatives. Much of the work recorded in Burton and Gibson's first paper in this series was in progress before Wieland and Rheinheimer's publication in 1921.[72]

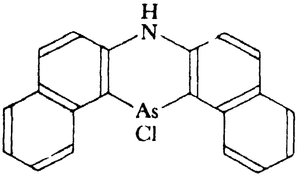
For the preparation of 10-chloro-5,10-dihydrophenarsazine by the condensation of diphenylamine and arsenic trichloride, Burton and Gibson[70] recommend the use of *o*-dichlorobenzene as a solvent; on cooling, the 10-chloro compound crystallizes directly. They point out that this

---

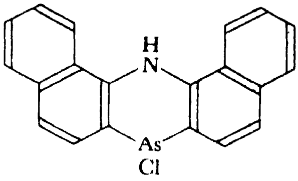
[78] Burton and Gibson, *J. Chem. Soc.*, **1926**, 464.
[79] Burton and Gibson, *J. Chem. Soc.*, **1927**, 247.
[80] Burton and Gibson, *J. Chem. Soc.*, **1927**, 2499.
[81] Gibson and Johnson, *J. Chem. Soc.*, **1928**, 2204.
[82] Gibson and Johnson, *J. Chem. Soc.*, **1929**, 767.
[83] Gibson and Johnson, *J. Chem. Soc.*, **1929**, 1080.
[84] Gibson and Johnson, *J. Chem. Soc.*, **1929**, 1229.
[85] Gibson and Johnson, *J. Chem. Soc.*, **1929**, 1473.
[86] Gibson and Johnson, *J. Chem. Soc.*, **1929**, 1621.
[87] Gibson and Johnson, *J. Chem. Soc.*, **1929**, 2743.
[88] Gibson and Johnson, *J. Chem. Soc.*, **1930**, 1124.
[89] Gibson, Hiscocks, Johnson, and Jones, *J. Chem. Soc.*, **1930**, 1622.
[90] Elson and Gibson, *J. Chem. Soc.*, **1931**, 294.
[91] Elson and Gibson, *J. Chem. Soc.*, **1931**, 2381.
[92] Gibson and Johnson, *J. Chem. Soc.*, **1931**, 2518.
[93] Gibson and Johnson, *J. Chem. Soc.*, **1931**, 3270.

10-chloro compound has a remarkable facility for separating from solution with solvent of crystallization; it will crystallize with a definite proportion of acetic acid, *sym*-tetrachloroethane, chlorobenzene, *o*-dichlorobenzene, acetone, carbon tetrachloride, or even arsenic trichloride. Furthermore, the "oxide" or anhydride (V) can be prepared by heating diphenylamine with arsenious oxide in the presence of phosphoric anhydride above 130°.

They showed[70] that when a mixture of 2-naphthylamine and arsenic trichloride was heated in *o*-dichlorobenzene, 1,2,8,9-dibenz-10-chloro-5,10-dihydrophenarsazine (XVI), R.I. 3190, was obtained as yellow crystals, m.p. 355°. It is clear from this result that under these circumstances the 2-naphthylamine must first have formed di-(2-naphthyl)amine, which then gave the normal phenarsazine condensation with arsenic trichloride. 1-Naphthylamine would not condense in this way, and di-(1-naphthyl)amine had to be employed directly for the preparation of the 3,4,6,7-dibenz isomeride (XVII), R.I. 3191, yellowish-brown crystals, m.p. 278–279°.



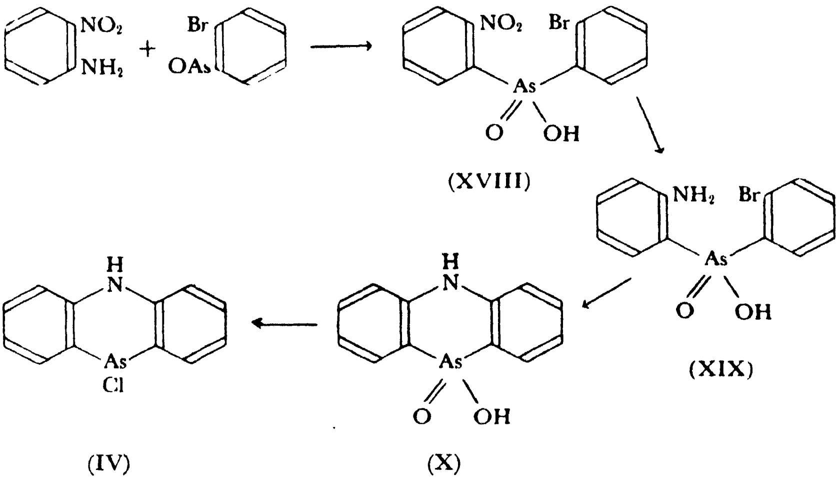
(XVI)



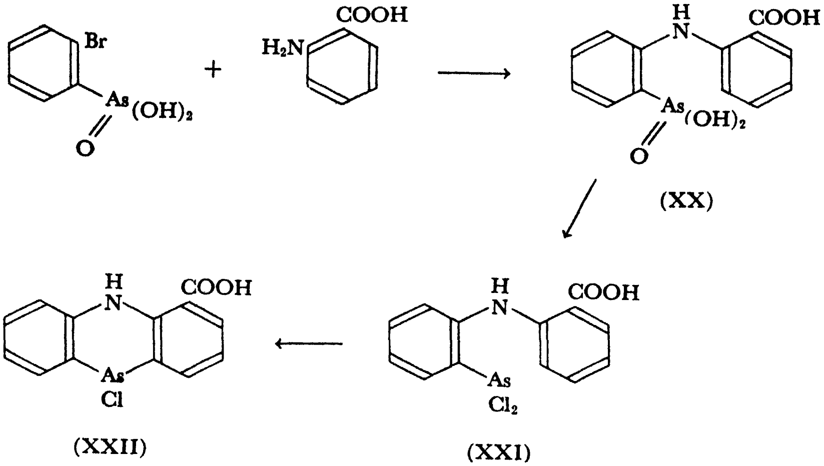
(XVII)

It will be realized that although the diphenylamine – arsenic trichloride condensation places the constitution of 10-chloro-5,10-dihydrophenarsazine (III) beyond reasonable doubt, it does not provide an absolute proof of this structure. The following alternative synthesis[70] was developed by Burton and Gibson to provide this proof.

o-Nitraniline was diazotized and then coupled with *o*-bromophenyl arsenoxide under the usual conditions of the Bart reaction to give 2-bromophenyl-2′-nitrophenylarsinic acid (XVIII). This compound was reduced to the 2′-aminophenyl derivative (XIX), which when heated in amyl alcohol with potassium carbonate and copper powder underwent the normal Ullmann condensation with the formation of phenazarsinic acid (X), which on reduction gave the 10-chloro derivative (IV). This constitutes the first unambiguous demonstration of the structure of the 10-chloro compound (IV).



A third synthesis[79] was developed initially for the preparation of 10-chlorophenarsazines carrying carboxylic acid groups substituted in the benzene rings. These derivatives cannot readily be prepared by the arsenic trichloride condensation method because it is difficult to obtain the necessary carboxydiphenylamines. For this purpose, Burton and Gibson condensed *o*-bromophenylarsonic acid with, for example, anthranilic acid by boiling the two reactants in nitrobenzene solution with potassium carbonate and copper powder. This Ullmann condensation thus furnished 2-carboxydiphenylamine-2′-arsonic acid (XX), which when reduced by sulfur dioxide (and a trace of iodine) in ethanolic solution gave the dichloroarsine (XXI). However, this compound was unstable, but when either boiled in acetic acid solution, or alternatively boiled with sodium hydroxide solution and then treated with hydrochloric acid, it furnished 4-carboxy-10-chloro-5,10-dihydrophenarsazine (XXII), yellow needles, m.p. 243°.



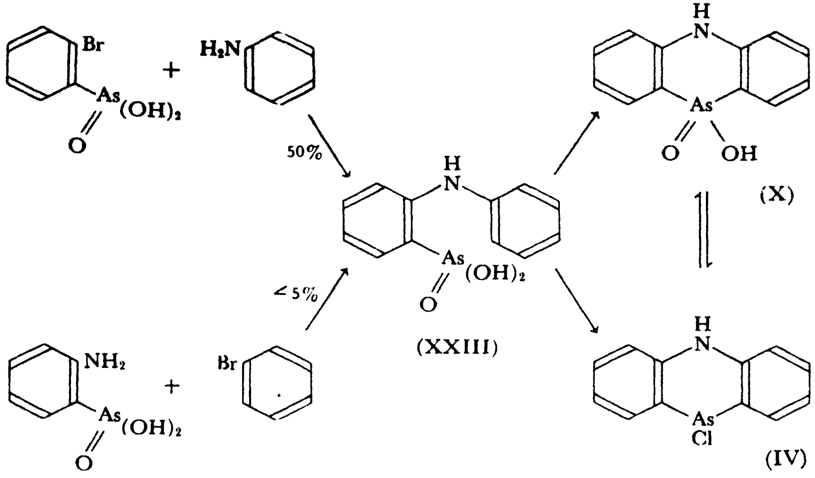
(XX)

(XXII)

(XXI)

This method of synthesis was subsequently widely used for the preparation of various substituted phenarsazines.[80,81,86] Its utility depends primarily on the reactivity of the bromine atom, which in turn determines the yield obtained in the Ullmann condensation. A study[80] was therefore made of the factors which affect the reactivity of this atom. As a simple example, when *o*-bromophenyl arsonic acid and aniline were condensed together under the usual conditions, a 50% yield of diphenylamine-2-arsonic acid (XXIII) was obtained. When, however, *o*-aminophenylarsonic acid was condensed with bromobenzene, a yield of less than 5% of the arsonic acid (XXIII) was obtained. This acid when boiled with hydrochloric acid underwent cyclization to phenazarsinic acid (X) and when reduced with sulfur dioxide in hydrochloric acid solution gave the 10-chloro compound (IV). Since the phenazarsinic acid can be reduced to the 10-chloro compound, and the latter oxidized back to the acid, the relationship of these compounds was clearly demonstrated.

Burton and Gibson had earlier[70] cast doubts on the statement of Wieland and Rheinheimer[72] that arsenic chloride condensed with diphenylmethylamine to give the 5-methyl derivative (XIII). They repeated this experiment but obtained only the unmethylated 10-chloro-5,10-dihydro compound (IV), and all their attempts to methylate this

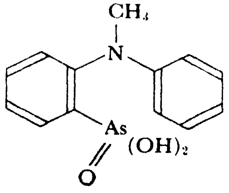


(XXIII)

(X)

(IV)

10-chloro compound or to synthesize the 5-methyl derivative by an indirect route had failed.[70] They concluded therefore that Wieland and Rheinheimer's product (XIII) was really a sample of 10-chloro-5,10-dihydrophenarsazine, the diphenylmethylamine having become demethylated in the course of the condensation. This conclusion received



(XXIV)

strong confirmation when it was found later that *o*-bromophenylarsonic acid could be condensed with monomethylaniline to give diphenylmethylamine-2-arsonic acid (XXIV), but that the latter could not be cyclized to give either the 5-methylphenazarsinic acid or the 10-chloro-5-methylphenarsazine.[80] This result is in striking contrast to the ready cyclization of the unmethylated arsonic acid (XXIII).

Burton and Gibson also questioned the accuracy of Lewis and Stiegler's claim[77] that 2-chlorovinyl-dichloroarsine would condense with diphenylamine to give the 10-(2-chlorovinyl)-phenarsazine (XV) and with phenyl-1-naphthylamine to give the corresponding 3,4-benz-10-(2-chlorovinyl)-phenarsazine (XIV, R = CH:CHCl). They repeated these experiments and in each case isolated only the corresponding 10-chlorophenarsazine in low yield. This would indicate that the chlorovinyl arsine had possibly undergone dismutation, and that the arsenic trichloride had then performed the normal cyclization.

$$2(\mathrm{ClCH\cdot CH})\mathrm{AsCl_2} \rightleftharpoons (\mathrm{ClCH.CH})_2\mathrm{AsCl} + \mathrm{AsCl_3}$$

Burton and Gibson therefore investigated in some detail the reaction between phenyldichloroarsine and diphenylamine.[78] They found that the product was always 10-chloro-5,10-dihydrophenarsazine (III), while free benzene was liberated during the reaction. It would appear that the reaction might follow one of the three possible routes:

$$\mathrm{C_6H_5AsCl_2} + (\mathrm{C_6H_5})_2\mathrm{NH} \longrightarrow \mathrm{ClAs:(C_6H_4)_2:NH} + \mathrm{C_6H_6} + \mathrm{HCl} \tag{1}$$

$$2\mathrm{C_6H_5AsCl_2} \longrightarrow (\mathrm{C_6H_5})_2\mathrm{AsCl} + \mathrm{AsCl_3} \tag{2a}$$

$$\mathrm{AsCl_3} + (\mathrm{C_6H_5})_2\mathrm{NH} \longrightarrow \mathrm{ClAs:(C_6H_4)_2:NH} + 2\mathrm{HCl} \tag{2b}$$

$$(\mathrm{C_6H_5})_2\mathrm{AsCl} + \mathrm{HCl} \longrightarrow \mathrm{C_6H_5AsCl_2} + \mathrm{C_6H_6} \tag{2c}$$

$$\mathrm{C_6H_5AsCl_2} + (\mathrm{C_6H_5})_2\mathrm{NH} \longrightarrow \mathrm{C_6H_5As:(C_6H_4)_2:NH} + \mathrm{HCl} \tag{3}$$

$$\mathrm{C_6H_5As:(C_6H_4)_2:NH} + \mathrm{HCl} \longrightarrow \mathrm{ClAs:(C_6H_4)_2:NH} + \mathrm{C_6H_6}$$

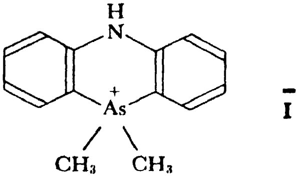
Of these routes, the reactions under (2) would appear to be most probable, with possibly both the diphenyl- and monophenyl-chloroarsines reacting to some extent with the hydrogen chloride to liberate benzene.

Precisely similar results were obtained when phenyldichloroarsine was condensed with phenyl-*p*-tolylamine, di-*p*-tolylamine, and phenyl-1-naphthylamine[78]: the products were 10-chloro-1-methyl-5,10-dihydrophenarsazine, 10-chloro-1,8-dimethyl-5,10-dihydrophenarsazine, and 3,4-benz-10-chloro-5,10-dihydrophenarsazine (XIV, R = Cl), respectively. No indication of the formation of a 10-phenylphenarsazine could be obtained in any of these experiments. It would appear, therefore, that in spite of the earlier claims the diphenylamine – arsenic trichloride condensation cannot be modified to allow the direct preparation of 5,10-

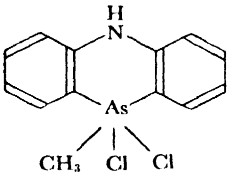
dihydrophenarsazines having alkyl or aryl groups substituted in either the 5 or the 10 position.[94]

The preparation of 10-alkyl (and aryl) derivatives of phenarsazine was first achieved by Aeschlimann,[95] who showed that 10-chloro-5,10-dihydrophenarsazine would react with two molecular equivalents of a Grignard reagent, for example, methylmagnesium iodide, to give the 10-methyl-5,10-dihydrophenarsazine, with the liberation of one molecule of the corresponding hydrocarbon (*e.g.*, methane). By this method he was able to prepare the 10-methyl compound, almost colorless needles, m.p. 105°; the 10-ethyl compound, m.p. 75°; and the 10-phenyl compound, m.p. 142°.

These compounds now contain true tertiary arsine groups, and therefore unite with alkyl iodides to give the corresponding arsonium salts. The 10-methyl compound will combine with methyl iodide even in the cold to give the crystalline 10,10-dimethyl-5,10-dihydrophenarsazonium iodide (XXV). When heated in a vacuum, this salt loses methyl iodide, regenerating 10-methyl-5,10-dihydrophenarsazine.



(XXV)



(XXVI)

The above 10-methyl, -ethyl, and -phenyl compounds were later prepared by the same method also by Seide and Gorski,[96] who in addition prepared the 10-(1-naphthyl)-5,10-dihydrophenarsazine, m.p. 154–155°. They showed that the 10-methyl and 10-phenyl compounds added on chlorine to give arsine dichlorides such as (XXVI), which on heating lost the 10-alkyl or -aryl group, giving 10-chloro-5,10-dihydrophenarsazine, presumably with the loss of methyl chloride and chlorobenzene, respectively.

---

[94] Gibson, *J. Am. Chem. Soc.*, **53**, 376 (1931).
[95] Aeschlimann, *J. Chem. Soc.*, **1927**, 413.
[96] Seide and Gorski, *Ber.*, **62**, 2186 (1929).

The chemistry of quaternary salts of type (XXV) and their corresponding hydroxides, and also of the betaines that are obtained by the addition of chloracetic acid to the tertiary arsines followed by loss of hydrogen chloride has been investigated by Razuvaev and his co-workers.[97,98]

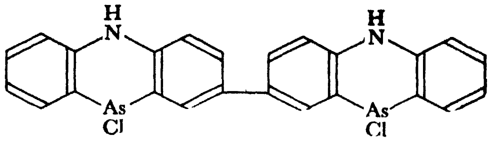
It is noteworthy that although 10-chloro-5,10-dihydrophenarsazine and phenazarsinic acid apparently do not react with nitrous acid to give the 5-nitroso derivatives, the 10-alkyl- and 10-aryl-5,10-dihydrophenarsazines will do so if the conditions of nitrosation are carefully controlled. Thus Razuvaev, Godina, and Yemelyanova[98a] have shown that the addition of hydrochloric acid to an alcoholic solution containing 10-methyl-5,10-dihydrophenarsazine and sodium nitrite affords the 5-nitroso derivative, m.p. 108–110 °; the 10-ethyl-5,10-dihydrophenarsazine similarly gives the 5-nitroso derivative as a viscous liquid, and the 10-phenyl-5,10-dihydrophenarsazine gives the 5-nitroso derivative, m.p. 143–145 °. These 5-nitroso derivatives are unstable, however, and in alcoholic or benzene solution are readily converted to resinous red products, which appear to contain both nitro derivatives and oxidation derivatives.

It will be obvious that Burton and Gibson's third synthesis of the phenarsazine system by the use of *o*-bromophenylarsonic acid opens up a wide field for the preparation of complex phenarsazines, particularly those having other rings fused onto the phenarsazine system itself. Many of these have been prepared by Gibson and his co-workers. The following are cited to illustrate the potentialities of this synthesis. When benzidine[81] was condensed with *o*-bromophenylarsonic acid, and the resulting diarsonic acid then cyclized, it gave 2,2′-bis(10-chloro-5,10-dihydrophenarsazine) (XXVII). *o*-Phenylenediamine,[81] similarly treated gave the pentacyclic derivative (XXVIII), R.I. 3189, and isomeric compounds were obtained from *m*- and *p*-phenylenediamine. 5-Aminoacenaphthene[86] gave the derivative (XXIX), R.I. 3138, as orange-red plates, m.p. 241 °.

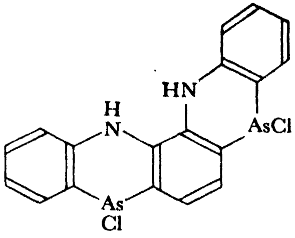
Slater[98b] has described a particularly interesting application of this synthesis. 8-Amino-5-nitroquinoline condenses with *o*-bromophenylarsonic acid in amyl alcohol solution to give *o*-(5′-nitro-8′-quinolylamino)-phenylarsonic acid (XXX). This acid, when reduced in ethanolic

---

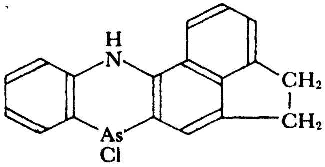
[97] Razuvaev and Malinovski, *J. Gen. Chem. U.S.S.R.*, **5**, 570 (1935).
[98] Razuvaev, Malinovski, and Arkina, *J. Gen. Chem., U.S.S.R.*, **5**, 575 (1935).
[98a] Razuvaev, Godina, and Yemelyanova, *Ber.*, **65**, 667 (1932).
[98b] Slater, *J. Chem. Soc.*, **1931**, 1939.



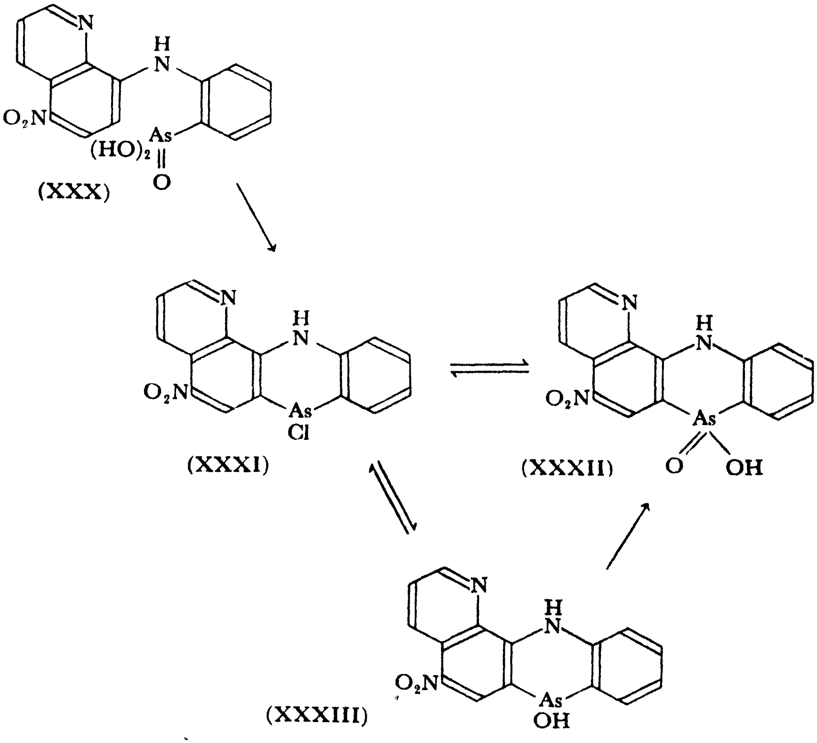
(XXVII)



(XXVIII)



(XXIX)



(XXX)

(XXXI)

(XXXII)

(XXXIII)

hydrogen chloride with sulfur dioxide, readily cyclizes to give the hydrochloride of the pyridophenarsazine (XXXI), R.I. 2599, as deep red feathery crystals, m.p. 258–260°. This compound, when oxidized in acetic acid solution with hydrogen peroxide, gives the phenazarsinic acid (XXXII), a process that can be reversed by a further application of the hydrogen chloride – sulfur dioxide reduction. The azarsinic acid is, of course, an amphoteric compound, and solutions of its sodium and potassium salts show all the remarkable color changes on dilution and on the addition of concentrated alkali that Gibson and Johnson[84] have described for more simple 2-nitrophenazarsinic acids.

When the chlorophenarsazine (XXXI) is treated with aqueous alkali, or even when it is boiled with water, it undergoes hydrolysis to the corresponding phenazarsinous acid (XXXIII). This change can be reversed either directly by treatment with hydrochloric acid, or indirectly by oxidation of the azarsinous acid to the azarsinic acid (XXXII) followed by reduction of the latter to the chloro-compound (XXXI) as described above.

For an account of phenarsazines having methyl groups substituted in the benzene ring, see in particular footnotes 82, 84, 85, 87, and 88; for the chloro derivatives, footnote 90; for the nitro derivatives, footnotes 84 and 93; for those having the carboxylic acid group, footnote 79, and for those having the —COCH$_3$ group substituted in the benzene ring, footnote 91.

For an account of the condensation of the 10-chloro compound (IV) with 2-mercaptoethanol in the presence of ethanolic potash to give 10-(2-hydroxyethylthio)-5,10-dihydrophenarsazine, m.p. 164–166°, see Ruggeberg, Ginsburg, and Cook.[62]

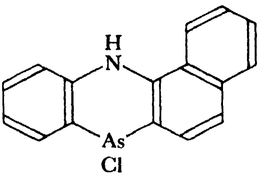
Many 10-substituted 5,10-dihydrophenarsazines on reduction (particularly in the presence of acids, for example, in hot formic acid solution) give intensely colored solutions of the "meriquinoid" derivatives, which have been investigated in some detail by Razuvaev and his co-workers.[98c–h] The production of these colored products is sometimes dependent on the temperature, the color becoming more intense as the temperature rises, and fading again as the solution cools, a property which suggests dissociation to free radicals. In other cases, the colored product will slowly

---

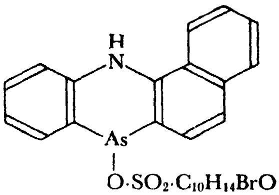
[98c] Razuvaev, *Ber.*, **62**, 605 (1929); *J. Russ. Phys. Chem. Soc.*, **61**, 3 (1929).
[98d] Razuvaev, *Ber.*, **62**, 1208 (1929).
[98e] Razuvaev and Malinovski, *Ber.*, **62**, 2675 (1929).
[98f] Razuvaev and Benediktov, *Ber.*, **63**, 343 (1930).
[98g] Razuvaev, *Rec. Trav. Chim.*, **50**, 900 (1931).
[98h] Razuvaev and Malinovski, *Ber.*, **66**, 463 (1933).

absorb atmospheric oxygen with the formation of the original 10-substituted 5,10-dihydrophenarsazine or of the corresponding phenazarsinic acid. The structure of the intermediate colored "meriquinoid" compound remains uncertain, and it is probable that the processes involved in the color formation may vary with the particular phenarsazine derivative investigated.

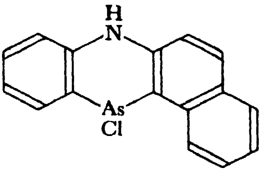
It should be added that the phenarsazines have been employed to obtain evidence for the stereochemistry of the 3-covalent arsenic atom. Allen, Wells, and Wilson[99] have boiled 3,4-benz-10-chloro-5,10-dihydrophenarsazine (XXXIV), R.I. 2602, with an equivalent of silver *d*-bromocamphor sulfonate in acetic anhydride. The silver chloride was filtered off, the filtrate evaporated to dryness in a vacuum, and the residue recrystallized from ethanol containing 5% water. Four fractions were obtained: (1) crystals, m.p. 211–212°; (2) crystals, m.p. 200°; (3) a yellow powder, m.p. 188–189°, (4) brown prisms, m.p. 182–183°. Fractions (1) and (2) were halogen-free and were optically inactive. Fractions (3) and (4) gave analytical values for the bromocamphor sulfonate (XXXV) and were optically active, fraction (3) having $[\alpha]_D + 59.5°$ and fraction (4) having $[\alpha]_D + 35.1°$ in 95% ethanolic solution. The rotations were stable if the solutions were kept in the dark, but exposure to light caused slow chemical decomposition with change of rotation. The authors consider that fractions (3) and (4) are diastereo isomerides, and they calculated that the phenarsazine portion of the molecule (XXXV), *i.e.*, the molecule minus the bromocamphor sulfonate group, has $[\alpha]_D + 25.6°$ in fraction (3) and $-24.9°$ in fraction (4). The initial 10-chloro compounds could not be regenerated from these bromo-



(XXXIV)



(XXXV)



(XXXVI)

---

[99] Allen, Wells, and Wilson, *J. Am. Chem. Soc.*, **56**, 233 (1934).

camphor sulfonates. No similar fractions were obtained by the similar treatment of 1,2-benz-10-chloro-5,10-dihydrophenarsazine (XXXVI) R.I. 2601.

It is very difficult to assess the theoretical significance of these results, particularly as the experimental data recorded in the paper are extremely scanty. It is clear that the rotations actually observed under the stated conditions were exceedingly small, in fact far too small to justify the specific rotations being calculated to three significant figures. Furthermore, the bromocamphor sulfonate group in (XXXV) must be covalently bound to the arsenic, a most unusual type of linkage for an oxy acid radical. In view of this covalent bond, however, the rotation of the compound (XXXV) will not necessarily be the sum of that of the phenarsazine portion and that of the bromocamphor sulfonate group—this additive relationship applies only to salts of strong acids and bases in dilute solution in ionizing solvents; consequently, the basis of the calculation of the rotation of the phenarsazine portion of the molecule is uncertain. Moreover, the combined yield of fractions (3) and (4) amounted to only about 10% of that theoretically possible, and the identity of fractions (1) and (2) was apparently not determined. However, if the phenarsazine portion of the molecule is contributing to the total activity, this contribution may be due either to the 10-substituent being above or below the plane of the cyclic phenarsazine system, or to the molecule being folded about the N—As axis: either property would render the molecule devoid of symmetry. The possibility of a folded molecule is discussed fully in connection with the phenoxarsines (p. 108), the arsanthrenes (p. 121), and the phenoxstibines (p. 154), where the evidence is considerable.

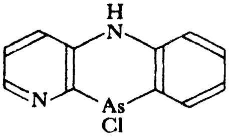
It has already been stated (p. 81) that 10-chloro-5,10-dihydrophenarsazine (IV), often known as "adamsite" in the United States, has an irritating effect on the mucous membrane similar to that of diphenylmonochloroarsine. Its physiological effects have therefore led to a careful study of its potential value as a weapon in chemical warfare. For this purpose, it would almost certainly be used as a smoke or suspension because the normal stable rhombic form has m.p. 195°, although Fischer[100] states that it also exists in two metastable forms, one monoclinic, m.p. 186°, and the other probably triclinic, m.p. 182°. For data regarding its toxic properties and those of other irritant compounds, and for an assessment of its comparative value as a chemical warfare agent, see Mielenz[101] and others.[102] For an account of the size of particles of the 10-chloro compound in smoke, particularly compared with diphenylmonochloroarsine, see Redlinger.[103] The detection, occurrence, and the safety measures to be observed in manipulating the 10-chloro compound have been described by Leroux,[104] who has collected a considerable number of references to this subject.

---

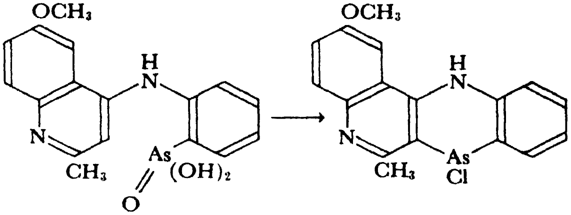
[100] Fischer, *Mikrochemie*, **12**, 257 (1932).

Azaphenarsazines

It will be clear that a number of compounds analogous to the phenarsazines but having one of the benzene rings replaced by a pyridine ring, for example, 1-aza-10-chloro-5,10-dihydrophenarsazine (I) should be capable of existence. A number of isomers is now possible, dependent on the position of the pyridyl nitrogen atom relative to the central heterocyclic ring. In some cases this ring system can be readily prepared. Thus, Slater[105] has shown that the arsonic acid (II), *i.e.*, *o*-(6′-methoxy-2′-methyl-4′-quinolylamino)-phenylarsonic acid, when reduced in ethanolic hydrochloric acid solution with sulfur dioxide gives the compound (III), R.I. 2600, yellow crystals, m.p. 245–247°. This compound can be recrystallized from hot water and the chlorine atom has therefore remarkably low reactivity. When the compound (III) is oxidized in acetic acid solution with hydrogen peroxide it gives the corresponding



(I)



(II) (III)

---

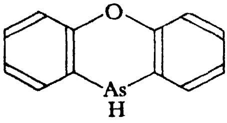
[101] Mielenz, *Gasschutz u. Luftschutz*, **2**, 10 (1932).
[102] Anon., *Gasschutz u. Luftschutz*, **2**, 264 (1932).
[103] Redlinger, *Gasschutz u. Luftschutz*, **2**, 263 (1932).
[104] Leroux, *Rev. hyg. et med. prévent.*, **57**, 81 (1935).
[105] Slater, *J. Chem. Soc.*, **1931**, 107.

azarsinic acid, having the :AsO(OH) group; this acid is an amphoteric compound insoluble in most neutral organic solvents, but soluble in sulfuric acid, giving a brilliant blue fluorescence. When this azarsinic acid is treated with phosphorus oxychloride, it furnishes the azarsinyl chloride, having the :AsOCl group, m.p. 165–167°.

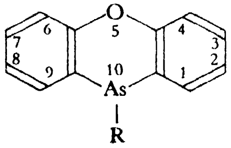
Six-Membered Ring Systems Containing Carbon, Arsenic, and Oxygen

Phenoxarsines

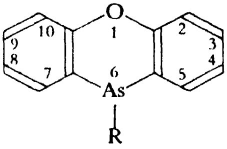
The parent phenoxarsine (I), R.I. 1828, is at present unknown, and all phenoxarsines hitherto prepared are compounds of type (II) or their derivatives. Various systems of numbering the constituent atoms have been adopted by chemists in the past. In this work the system given in (II) is adopted throughout, for the same reasons that the analogous numbering is used in the 5,10-dihydrophenarsazines, namely, that this system is the one adopted in the *Ring Index* and the one normally employed in other similar types of tricyclic compounds. It should be noted, however, that the system of numbering given in (III) is that adopted in *Chemical Abstracts*.



(I)



(II)



(III)

The phenoxarsines, like the phenarsazines, owe their development very largely to the conditions obtaining in World War I. Their first record in open publication was by Lewis, Lowry, and Bergeim,[106] who made a number of derivatives by a method initiated by Turner[107] and sent to them by Sir William Pope in a Chemical Warfare Communication. These workers, following Turner's preparative method, showed that

---

[106] Lewis, Lowry, and Bergeim, *J. Amer. Chem. Soc.*, 43, 893 (1921).
[107] Turner, Dissertation submitted for D.Sc. Degree, London University, 1920.

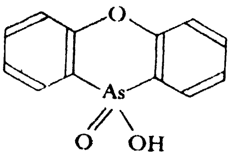
10-chlorophenoxarsine (II, R = Cl) could be readily prepared by refluxing equivalent quantities of diphenylether and arsenic trichloride together with a small quantity of aluminum chloride until the temperature reached 200°. The product was cooled, and the crystalline 10-chlorophenoxarsine then filtered off. If the mother liquor were then further refluxed, a second crop could be obtained, the total yield being 46%.

The 10-chloro compound thus obtained had an irritating action on the mucous membrane, particularly if the compound was dissolved in a volatile solvent, although Lewis, Lowry, and Bergeim[106] state that it is less irritating to the nose, throat, and skin than is 10-chloro-5,10-dihydrophenarsazine.

10-Chlorophenoxarsine is a stable compound not readily affected by boiling water or by 10% aqueous sodium hydroxide solution. The chloro group, however, can be readily replaced by other groups. Thus, treatment in methanol solution with the appropriate sodium salt gives 10-bromophenoxarsine, m.p. 128°, 10-iodophenoxarsine, m.p. 144°, and 10-thiocyanatophenoxarsine (II, R = ·CNS), m.p. 129°: these three compounds all form yellow crystals.

When the 10-chloro compound is heated with alkalis, or with sodium methoxide or ethoxide, or treated with ethanolic ammonia, it gives the "oxide," $O:(C_6H_4)_2:As{\cdot}O{\cdot}As:(C_6H_4):O$, "needle-like fibers," m.p. 182°; this compound, which is really the anhydride of 10-hydroxyphenoxarsine (II, R = OH), is soluble in all the common organic solvents, but insoluble in water or alkalis. When treated with the hydrogen halides, it is converted to the corresponding 10-halogenophenoxarsine. This is the best method of preparing the pure 10-bromo compound. When the 10-chloro compound in ethanol is treated with hydrogen sulfide, it forms the corresponding sulfide, $O:(C_6H_4)_2:As{\cdot}S{\cdot}As:(C_6H_4)_2:O$, pale yellow needles, m.p. 161°, which are insoluble in all common solvents except acetic acid. It is interesting to note that these solubility relationships are the reverse of those in the corresponding phenarsazine compounds, where the "oxide," $HN:(C_6H_4)_2:As{\cdot}O{\cdot}As:(C_6H_4)_2:NH$, is insoluble in most liquids but the corresponding sulfide is moderately soluble.

When 10-chlorophenoxarsine in aqueous suspension is treated with bromine, addition occurs at the arsenic atom, and if the mixture is then boiled to effect hydrolysis, phenoxarsinic acid, white needles (IV), m.p. 219°, is obtained.



(IV)

When the above "oxide" in ethanolic solution is reduced with phosphorous acid, it gives 10,10′-bisphenoxarsine, O : $(C_6H_4)_2$: As·As : (C_6H_4) : O. Lewis, Lowry, and Bergeim,[106] record this compound as yellow needles, m.p. 159°, which when exposed to air slowly gives a mixture of the "oxide" and phenoxarsinic acid, but which when dissolved in organic solvents undergoes rapid oxidation to the acid. Blicke, Weinkauff, and Hargreaves[108] prepared this compound under an atmosphere of carbon dioxide, and record m.p. 176–177°.

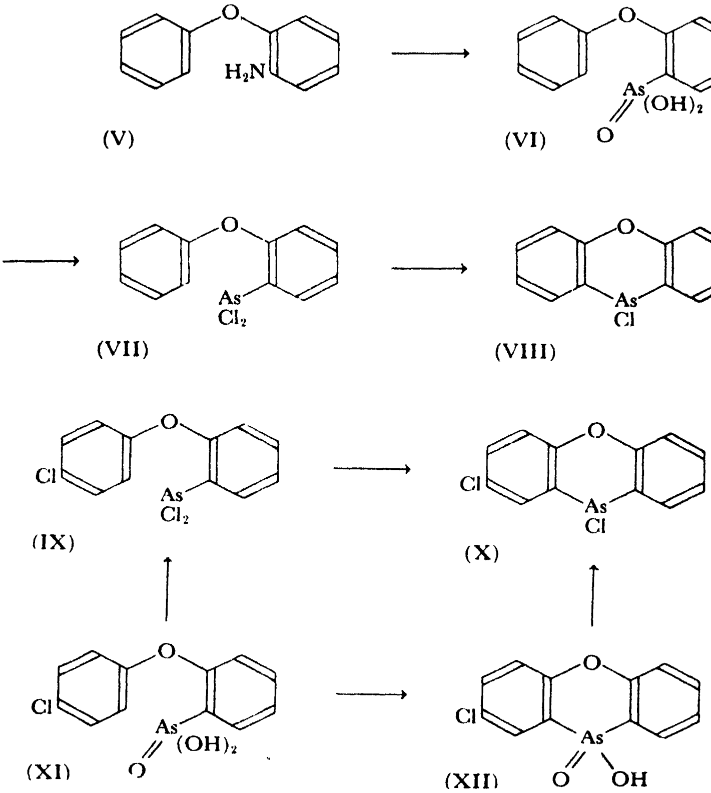
The statement by Lewis, Lowry, and Bergeim[106]—when the 10-chlorophenoxarsine is treated with magnesium ethyl iodide, it furnishes the 10-ethylphenoxarsine, as white needles, m.p. 218°—is in error (see below): the compound they isolated but did not analyze was almost certainly phenoxarsinic acid.

These properties, and the method of preparation, leave the structure of 10-chlorophenoxarsine reasonably certain. The following unambiguous synthesis, worked out by Turner and Sheppard,[109] provides, however, a complete proof of this structure. 2-Aminodiphenylether (V) was diazotized and converted by the Bart reaction to diphenylether-2-arsonic acid (VI), which when reduced in the usual way with sulfur dioxide in the presence of hydrochloric acid and a trace of iodide gave diphenylether-2-(dichloroarsine) (VII). This compound formed an orange-red oil, which on attempted distillation at 10 mm. pressure lost hydrogen chloride very readily with cyclization to 10-chlorophenoxarsine (VIII).

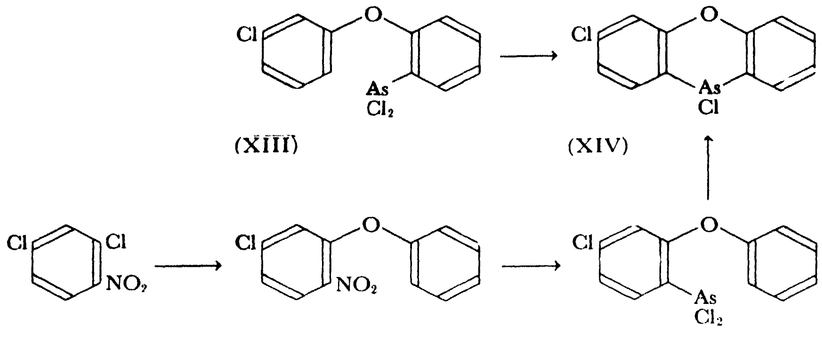
Roberts and Turner[110] have investigated the relative ease of cyclization of 2′-chlorodiphenylether-2-(dichloroarsine) and the 3′- and 4′-chloro isomers. The 2′-chloro compound thus gave 4,10-dichlorophenoxarsine, m.p. 99°, and the 4′-chloro compound (IX) gave 2,10-dichlorophenoxarsine (X), m.p. 144–145°. As an alternative route to the latter, the 4′-chloro-diphenylether-2-arsonic acid (XI), from which the dichloroarsine (IX) had been prepared, was warmed with sulfuric acid when cyclization readily occurred to give 2-chlorophenoxarsinic acid (XII), which when reduced in the usual way also furnished 2,10-dichlorophenoxarsine (X). In the case of 3′-chlorodiphenylether-2-(dichloroarsine) (XIII), cyclization might theoretically occur to give either 3,10-dichlorophenoxarsine (XIV) or 1,10-dichlorophenoxarsine, or a mixture of both. In practice, this cyclization occurred very readily and was found to give only one product, m.p. 125°, which was identified as the 3,10-dichloro isomer by the following synthesis. 2,4-Dichloronitrobenz-

---

[108] Blicke, Weinkauff, and Hargreaves, *J. Am. Chem. Soc.*, **52**, 780 (1930).
[109] Turner and Sheppard, *J. Chem. Soc.*, **127**, 544 (1925).
[110] Roberts and Turner, *J. Chem. Soc.*, **127**, 2004 (1925).



ene (XV) was condensed with potassium phenoxide in phenol solution to give 5-chloro-2-nitrodiphenylether (XVI). This compound was then reduced to the 2-amino compound, which when diazotized and subjected to the Bart reaction gave 5-chlorodiphenylether-2-arsonic acid, which in turn on reduction gave 5-chlorodiphenylether-2(dichloroarsine) (XVII). The latter then underwent the usual smooth cyclization, and



(XIII) (XIV)

(XV) (XVI) (XVII)

the product, which was necessarily 3,10-dichlorophenoxarsine, was found to be identical with that obtained by the cyclization of the isomeric dichloroarsine (XIII), and also with that obtained by reduction of the phenoxarsinic acid prepared by the cyclization of 3′-chlorodiphenylether-2-arsonic acid.

These workers found that under comparable conditions the unsubstituted dichloroarsine (VII) underwent cyclization more rapidly than the 3′-chloro compound (XIII), and the latter in turn reacted more readily than the 2′-chloro compound and the 4′-chloro compound (IX) which cyclized at approximately equal rates.

The effect of the nature and position of substituents upon the ease of ring closure in compounds of the type (IX) and (XIII) was subsequently examined in detail by Mole and Turner.[111] Their results, which were based on a quantitative study of the relative speeds of the ring closure in the various compounds examined, should be consulted by the interested reader. In the course of this work they isolated the following new derivatives of 10-chlorophenoxarsine:

---

[111] Mole and Turner, *J. Chem. Soc.*, **1939**, 1720.

Compound	M.p. °C.
10-Chloro-3-methylphenoxarsine	140–141
10-Chloro-4-methylphenoxarsine	90–91
10-Chloro-1,3-dimethylphenoxarsine	138–139
10-Chloro-1,4-dimethylphenoxarsine	146–147
10-Chloro-2,4-dimethylphenoxarsine	130–131
10-Chloro-2-methoxyphenoxarsine	108–109
10-Chloro-2-bromophenoxarsine	172–173

The ease of cyclization of a diphenylether-2-arsonic acid such as (XI) to the corresponding phenoxarsinic acid with sulfuric acid depends largely on the nature and position of the substituents in the benzene rings. This method is not practicable with diphenylether-2-arsonic acid itself, since sulfonation is the predominant reaction.[110] This behavior is of course in marked contrast to that of the diphenylamine-2-arsonic acids, which usually give ready cyclization to the corresponding phenazarsinic acid.

With regard to the earlier synthesis of 10-chlorophenoxarsine, *i.e.*, the condensation of arsenic trichloride with diphenylether, it should be noted that this reaction does not proceed unless aluminum chloride is present.[109] In this respect it is in marked contrast to the condensation of arsenic trichloride with diphenylamine (p. 80 ff.), which usually proceeds vigorously to form the corresponding phenarsazine without the presence of catalysts. In one other respect, however, these two condensations have a feature in common. Aeschlimann[112] has shown that phenyldichloroarsine, $C_6H_5AsCl_2$, reacts with diphenylether in the presence of aluminum chloride to give, not the expected 10-phenylphenoxarsine, but 10-chlorophenoxarsine. This is strictly analogous to Burton and Gibson's discovery[78] that phenyldichloroarsine reacts with diphenylamine to give 10-chloro-5,10-dihydrophenarsazine. In the phenoxarsine series, however, one might expect the formation of the 10-chloro compound to proceed more readily, because the aluminum chloride would promote the dismutation:

$$2C_6H_5AsCl_2 \rightleftharpoons (C_6H_5)_2AsCl + AsCl_3$$

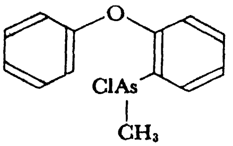
If the arsenic trichloride thus formed were condensing readily with the diphenylether, the production of the 10-chlorophenoxarsine would proceed smoothly. In the phenarsazine series, there is no aluminum chloride to hasten the attainment of the above equilibrium and hence the 10-chloro derivative is formed more slowly and (over a reasonable period of time) in low yield.

---

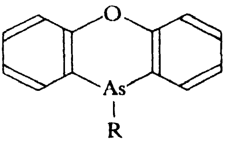
[112] Aeschlimann, *J. Chem. Soc.*, **127**, 811 (1925).

Aeschlimann[95] has attempted to prepare the 10-phenylphenoxarsine by heating 10-chlorophenoxarsine in benzene solution with aluminum chloride in the hope that a condensation of the Friedel-Crafts type would ensue, but the experiment proved fruitless.

The action of Grignard reagents on 10-chlorophenoxarsine has been investigated by Roberts and Turner,[113] and also by Aeschlimann.[95,112] It is noteworthy that the former were unable to prepare 10-methylphenoxarsine (XIX, R = CH_3) by the cyclization of 2-diphenylether-methylchloroarsine (XVIII): apparently the presence of the methyl group completely inhibits the cyclization which occurs so readily in the dichloroarsine. 10-Methyl and 10-ethylphenoxarsine can be readily prepared by the action of the appropriate Grignard reagent in ethereal solution on 10-chlorophenoxarsine; this reaction does not proceed so readily with phenylmagnesium bromide, and this Grignard reagent has to be boiled with the 10-chlorophenoxarsine in benzene solution for four hours to ensure conversion to the 10-phenylphenoxarsine.



(XVIII)



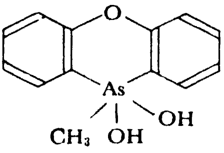
(XIX)

Aeschlimann[95,112] records the following properties for these three derivatives. 10-Methylphenoxarsine is an oil, b.p. 185°/20 mm., 198–200°/40 mm. When a solution in aqueous hydrogen peroxide is evaporated and the residue recrystallized, the dihydroxide (XX), m.p. 94° is obtained. The arsine readily gives a methiodide, systematically 10,10-dimethylphenoxarsonium iodide, m.p. 220° or 225° dependent on the rate of heating, and it also readily combines similarly with bromacetic acid to give 10-carboxymethyl-10-methylphenoxarsonium bromide

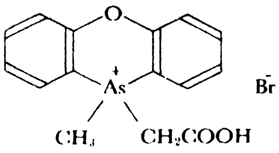
---

[113] Roberts and Turner, *J. Chem. Soc.*, **1926**, 1207.

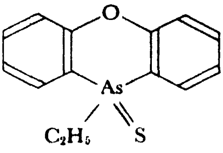
(XXI). 10-Ethylphenoxarsine is also an oil, b.p. 194°/20 mm., which could not be obtained in crystalline form. It also gives a dihydroxide, a methiodide, m.p. 186° or 193° dependent on the rate of heating, an ethiodide, m.p. 193°, and a bromacetic acid addition product analogous to (XXI). When 10-ethylphenoxarsine is boiled in carbon disulfide solution with one equivalent of sulfur, or when hydrogen sulfide is passed through an aqueous solution of the dihydroxide, 10-ethylphenoxarsine sulfide (XXII) is readily formed as colorless crystals, m.p. 109°.



(XX)



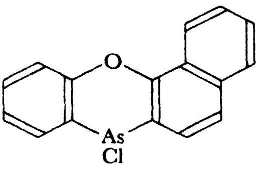
(XXI)



(XXII)

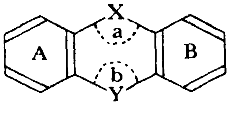
10-Phenylphenoxarsine occurs as colorless needles, m.p. 107°. It gives a methiodide, m.p. 175°, and a very hygroscopic oxide, m.p. 184°.

Derivatives of 10-chlorophenoxarsine having substituents in the benzene rings can be prepared by the use of suitably substituted diphenylethers. This has already been illustrated in the preparation of the dichloro derivatives (X) and (XIV).[110] As an example of a rather different type of derivative, Aeschlimann[112] has shown that phenyl-1-naphthylether condenses with arsenic trichloride in the presence of aluminum chloride to give 3,4-benz-10-chlorophenoxarsine (XXIII), R.I. 2604, m.p. 168°, but the yield was low.



(XXIII)

One of the most interesting features of the phenoxarsines is their stereochemistry, which is dependent on a factor (the relative orientation of the three constituent rings) which is also undoubtedly present in the arsanthrene and phenoxstibine series (pp. 117, 154). In the case of any tricyclic molecule of type (XXIV), in which A and B are true benzene rings, and in which X and Y are similar or different groups, it follows that



(XXIV)

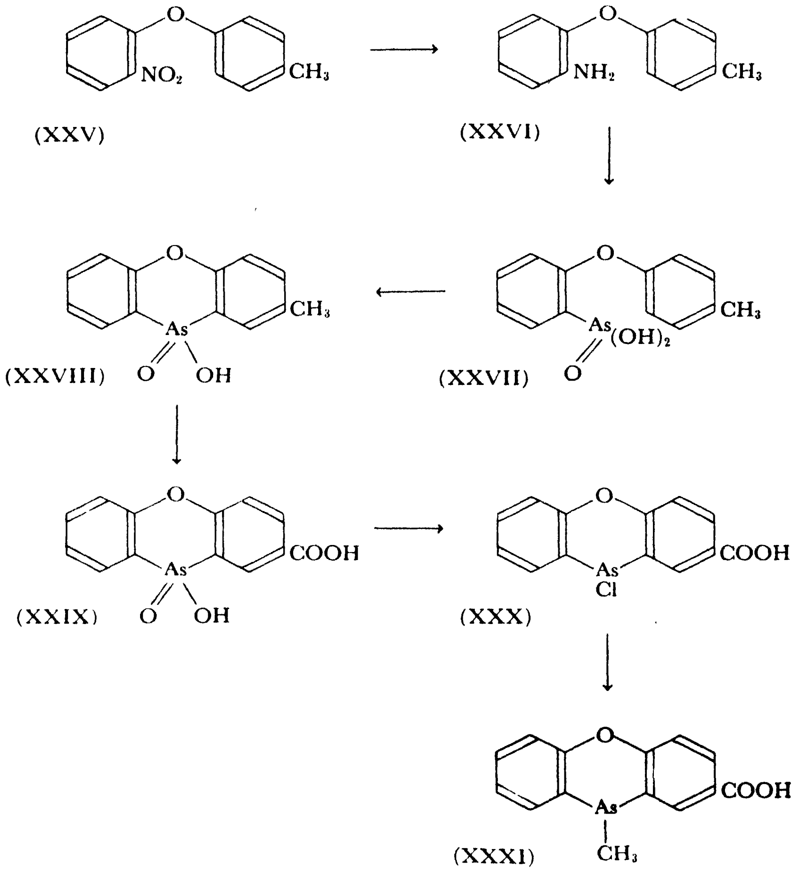
the three rings can be in one plane only if the intervalency angles *a* and *b* are 120° or closely approach this value; this factor has been discussed by Campbell, Le Fèvre, Le Fèvre, and Turner.[114] Now, in the case of arsine, AsH_3, and of the aliphatic tertiary arsines, AsR_3, there is considerable physical evidence that the intervalency angle at the arsenic atom is approximately 97°; for a summary of this evidence, see Chatt and Mann.[115] It would be anticipated, therefore, that the phenoxarsine molecule is folded about the O—As axis, and therefore the three rings cannot be uniplanar.

This point has been investigated by Lesslie and Turner.[116] For the preparation of a suitable compound, *o*-nitrophenyl-*p*-tolyl ether (XXV) was reduced to the *o*-amino compound (XXVI), which was then diazotized and by means of the Bart reaction converted to 2-(*p*-tolyloxy)phenylarsonic acid (XXVII). Lesslie and Turner found that this arsonic acid, if slowly added to ice-cold sulfuric acid, which was then warmed to 100° for 5 minutes, cooled, and poured onto ice, underwent satisfactory cyclization to 2-methylphenoxarsinic acid (XXVIII). On oxidation, the latter gave the 2-carboxy derivative (XXIX), which when reduced as usual by sulfur dioxide in the presence of hydrochloric acid, gave 10-chlorophenoxarsine-2-carboxylic acid (XXX). This compound, when treated with methyl magnesium iodide, gave 10-methylphenoxarsine-2-carboxylic acid (XXXI), R.I., 1828.

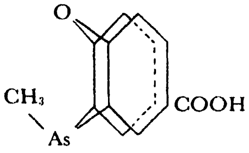
---

[114] Campbell, Le Fèvre, Le Fèvre, and Turner, *J. Chem. Soc.*, **1938**, 404.
[115] Chatt and Mann, *J. Chem. Soc.*, **1940**, 1184.
[116] Lesslie and Turner, *J. Chem. Soc.*, **1934**, 1170.

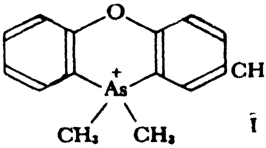
This acid was converted to its strychnine salt, which on recrystallization ultimately gave complete optical resolution. The 10-methyl acid (XXXI) was thus obtained in the *dextro* form having $[\alpha]^{20}_{5791}$ + 95.8°, $[\alpha]^{20}_{5461}$ + 111.5°, and in the *levo* form having $[\alpha]^{20}_{5791}$ − 96.0°, $[\alpha]^{20}_{5461}$ − 111.7°, all in ethanolic solution. This acid had considerable optical stability; thus an ethanolic solution could be boiled under pressure for several hours without racemization, and a solution in *N* NaOH solution could be heated at 100° for 6 hours without diminution of the optical activity.



Lesslie and Turner point out that there are two possible explanations of the optical activity of this acid. (*a*) If the molecule is folded about the O—As axis [as in (XXXII), in which the oxygen and the arsenic and the methyl group are depicted as lying in the plane of the paper, while the carboxyphenylene group projects above the plane of the paper, and the unsubstituted phenylene group projects below this plane], then the acid has no element of symmetry irrespective of the disposition of the methyl group. (*b*) If the tricyclic system were planar, the methyl group might lie above or below this plane and thus deny any element of symmetry to the molecule. It is known, however, that in arsine, AsH_3, the oscillation of the arsenic atom about the plane of the three hydrogen atoms is very rapid.[117] In the acid (XXXI), the position of the methyl group might be stabilized by the disposition of the ring system, but it is unlikely that this stabilization is so great that oscillation of the methyl group above and below the plane of the rings is entirely prevented; yet this condition would be essential in view of the great optical stability of the acid. The second explanation (*b*) is therefore almost certainly incorrect, and since the argument based on the intervalency angle at the arsenic atom points strongly to the first explanation (*a*), it is almost certain that this is correct and that the molecule is folded as shown in (XXXII). However, there is at present no evidence for the position of this methyl group relative to the O—As axis. It may lie on the opposite side of this axis relative to the *o*-phenylene groups, as shown in (XXXII), or on the same side as these groups but below them; in the latter case, its position will be comparable to that of the lower tolyl group in the arsanthrene compound (XIVA) (p. 122).



(XXXII)



(XXXIII)

---

[117] Sutherland, Lee, and Wu, *Trans. Faraday Soc.*, 35, 1373 (1939).

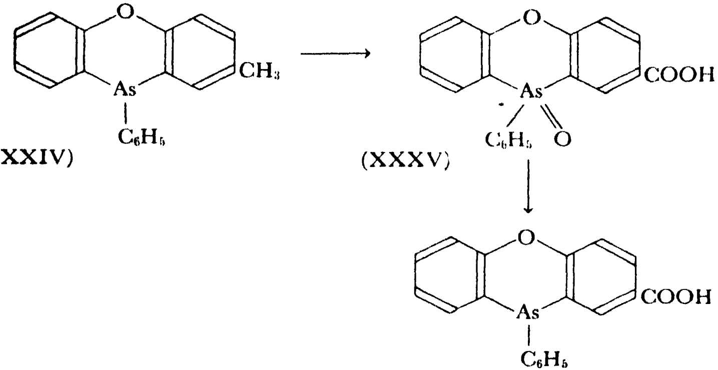
It is noteworthy, however, that when the acid was dissolved in methyl iodide, racemization occurred, slowly at first and then more rapidly as conversion to the methiodide, *i.e.*, 2-carboxy-10,10-dimethylphenoxarsonium iodide, proceeded. Similarly, racemization occurred with ethyl iodide, but more slowly owing to the lower reactivity of ethyl iodide and the more sluggish formation of the ethiodide. Now, if the acid had a *rigidly* folded structure as in (XXXII), the quaternary arsonium salt should also be devoid of any element of symmetry, and it would have been expected that the optical activity would have been retained. Lesslie and Turner point out, however, that since the formation of the methiodide or ethiodide is accompanied by the acquisition of a positive charge by the arsenic atom, the effective size of the latter must undergo simultaneous diminution, since the arsenic atom in an arsonium salt is probably little larger than an oxygen atom. They suggest, therefore, that it is almost inconceivable that a folded molecule such as (XXXII) could withstand the agitation accompanying this process without complete loss of optical activity.

In view of these results, Lesslie and Turner[118] have prepared the quaternary arsonium salts, 2,10,10-trimethylphenoxarsonium iodide (XXXIII), and the corresponding 2,10-dimethyl-10-phenyl derivative, but neither of these compounds gave any indication of optical resolution. It should be noted, however, that in all these four quaternary salts, the arsenic atom has now almost certainly become tetrahedral, and the intervalency angle at the arsenic atom within the ring has now increased from about 97° to about 109°. Although this latter value is still far short of 120°, it may in the phenoxarsine compounds weaken the rigidity of the folded structure. (No such weakening could be detected however in the arsanthrene compounds described later (p. 122), but in view of the absence of the oxygen atom they are not necessarily strictly comparable).

Lesslie and Turner[119] also have resolved the 10-ethylphenoxarsine-2-carboxylic acid, which had $[\alpha]_{5791} \pm 119°$ and $[\alpha]_{5461} \pm 139°$, and which also had great optical stability in organic solvents and in hot sodium hydroxide solution. With methyl iodide, however, it formed the corresponding methiodide, the process again being accompanied by complete racemization.

[118] Lesslie and Turner, *J. Chem. Soc.*, **1935**, 1051.
[119] Lesslie and Turner, *J. Chem. Soc.*, **1935**, 1268.

The 10-phenylphenoxarsine-2-carboxylic acid has also been investigated. Lesslie and Turner[120] were unable to prepare this compound by the action of phenyl magnesium bromide on the 10-chloro acid (XXX). Consequently they reduced the 2-methylphenoxarsinic acid (XXVIII) to the 10-chloro compound, which reacted readily with the above Grignard reagent to give 2-methyl-10-phenylphenoxarsine (XXXIV). On oxidation, this compound gave 2-carboxy-10-phenylphenoxarsine oxide (XXXV) and the latter then underwent smooth reduction to the required



(XXXIV)

(XXXV)

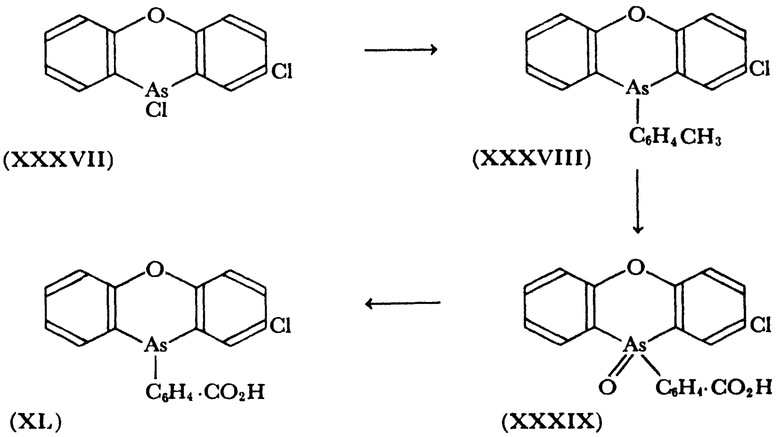
(XXXVI)

10-phenylphenoxarsine-2-carboxylic acid (XXXVI). This acid was resolved through its 1-phenylethylamine salts, and obtained in the two forms having $[\alpha]_{5791} \pm 223°$ and $[\alpha]_{5461} \pm 261°$; these values are notably higher than those of the 10-methyl and 10-ethyl homologs. The 10-phenyl acid also possessed great optical stability, and was unaffected by heating in ethanolic solution in a closed tube at 100° for 4 hours. Oxidation to the oxide (XXXV) caused complete racemization, however.

The optical properties of another compound in this series, namely, 10-*p*-carboxyphenyl-2-chlorophenoxarsine (XL), have recently been investigated by Lesslie.[120a] It had been suggested by Campbell[120b] that one of the factors contributing to the optical instability of 10-*p*-carboxyphenyl-2-methyl-phenoxstibine (page 155) may have been the heavy polar *p*-carboxyphenyl group in the 10 position, which might encourage inversion of the pyramidal configuration of the antimony atom. The analogous 10-*p*-carboxyphenyl-2-chlorophenoxarsine (XL) was therefore prepared and resolved into optically active forms in order to determine whether it also showed a similar optical instability.

---

[120] Lesslie and Turner, *J. Chem. Soc.*, **1936**, 730.
[120a] Lesslie, *J. Chem. Soc.*, **1949**, 1183.
[120b] Campbell, *J. Chem. Soc.*, **1947**, 4.



(XXXVII)

(XXXVIII)

(XL)

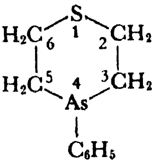
(XXXIX)

The acid was prepared by treating 2,10-dichlorophenoxarsine (XXXVII) with magnesium-*p*-tolyl bromide, whereby 2-chloro-10-*p*-tolylphenoxarsine (XXXVIII) was obtained. This compound, on oxidation, gave 10-*p*-carboxyphenyl-2-chlorophenoxarsine oxide (XXXIX), which, on reduction, gave the required 10-*p*-carboxyphenyl-2-chlorophenoxarsine (XL). This acid was resolved by the fractional crystallization of its strychnine and cinchonine salts, and obtained optically pure, having $[\alpha]_{5461}^{20^\circ}$ + 187.5 ° and −187.1 ° in chloroform. The acids were optically unaffected by boiling in alcohol or chloroform solution for 1 hour, or by boiling in 0.5 *N* sodium hydroxide solution for 3 hours, and it is clear, therefore, that in this series the optical stability is not weakened by the 10-*p*-carboxyphenyl group.

Six-Membered Ring Systems Containing Carbon, Arsenic, and Sulfur

Phenyl-thiarsine

Job, Reich, and Vergnaud[121] have shown that when phenylarsine, $C_6H_5AsH_2$, is boiled with an ether or benzene solution of ethyl magnesium bromide, ethane is evolved, and the Grignard reagent of constitution $C_6H_5As(MgBr)_2$ is formed. This reagent has been used for various synthetic purposes. These workers have found that when this reagent is boiled with 2,2′-dichlorodiethyl sulfide in benzene solution for one hour, the cyclic "phenyl-thiarsine" (I), R.I. 168, is formed. It is a solid compound, having m.p. 38°, b.p. 134°/14 mm., 177°/16 mm. It forms a monomethiodide (possibly on the arsenic or on the sulfur atom), m.p. 226°, and also forms a white mercuric chloride addition product, m.p. 181° and a yellow mercuric iodide addition product, m.p. 153°.



(I)

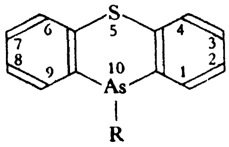
The further investigation of the properties of this compound would be of considerable interest.

Phenthiarsine

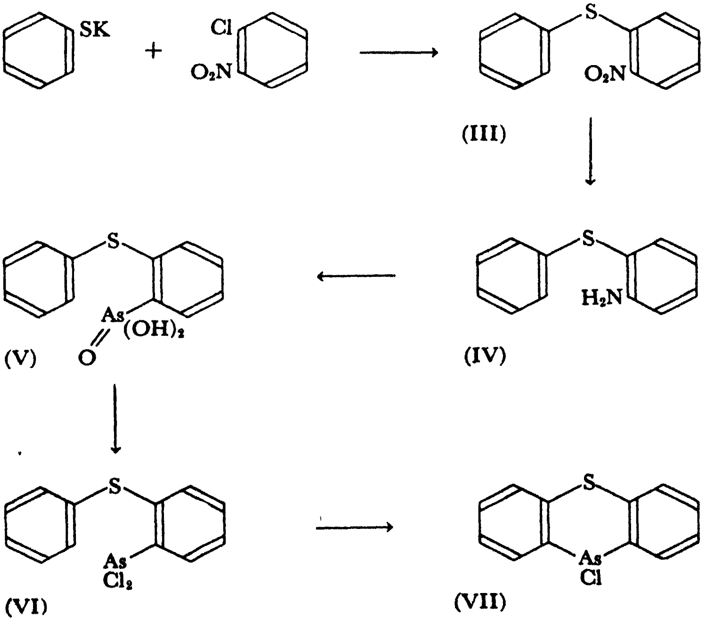
The phenthiarsines are the sulfur analogs of the phenoxarsines, and the ring system is numbered in the same way, *i.e.*, as shown in (II), R.I. 1830. At present, only the 10-chlorophenthiarsine (VII) appears to be known. It has been synthesized by Roberts and Turner[122] by the following method, which is strictly parallel to that used by Turner and Sheppard[109] for synthesizing the phenoxarsine analog. Potassium phenyl sulfide and *o*-chloronitrobenzene were heated together with copper bronze at 170–185° for 2 hours until the initial vigorous reaction had subsided and the condensation appeared complete. The 2-nitrodiphenyl sulfide (III) so obtained was reduced to the 2-amino derivative (IV), which was then diazotized and converted by the Bart reaction to diphenylsulfide-2-arsonic acid (V), m.p. 192–194°. Attempts to cyclize this with sulfuric

---

[121] Job, Reich, and Vergnaud, *Bull. soc. chim. France* [IV], **35**, 1404 (1924).
[122] Roberts and Turner, *J. Chem. Soc.*, **1926**, 1207.



(II)



acid to the arsinic acid failed. It was therefore reduced in hydrochloric acid by sulfur dioxide to give diphenylsulfide-2(dichloroarsine) (VI). This compound was a dark oil and could not be directly purified; it was therefore hydrolyzed to the arsine oxide, which on recrystallization gave white crystals, m.p. 187–189°, and this pure oxide was then converted back to the dichloroarsine (VI). This was then cyclized by heating at 200° while a stream of carbon dioxide was passed through; the 10-chlorophenthiarsine was thus obtained as sulfur-yellow crystals, m.p. 129–130°. It is noteworthy that the yield by this cyclization did not exceed 20%, whereas the yield of the 10-chlorophenoxarsine from the corresponding dichloroarsine under the same conditions was 60%.

Six-Membered Ring Systems Containing Carbon and Two Arsenic Atoms

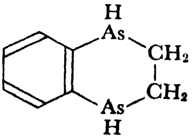
Ethylene-*o*-phenylenediarsine

The unknown ethylene-*o*-phenylenediarsine (I) can be regarded systematically as 4-arsa-1,2,3,4-tetrahydroarsinoline (*cf.* page 42); it is clearly the arsenic analog of tetrahydroquinoxaline, R.I. 978.

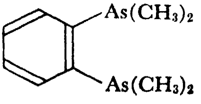
Derivatives containing this ring system have recently been obtained by Glauert and Mann.[122a] For this purpose, *o*-phenylenebis(dimethylarsine) (II), previously prepared by Chatt and Mann,[67] was heated with one molecular equivalent of ethylene dibromide, whereby the crystalline dimethobromide of 1,4-dimethylethylene-*o*-phenylenediarsine (III), alternatively named 1,1,4,4-tetramethylethylene-*o*-phenylenediarsonium dibromide, was readily obtained as colorless crystals, m.p. 245°.

Evidence that cyclization had actually occurred during this reaction to give the ring system shown in (III), and that the compound was not the isomeric monoarsonium salt (IV) was provided by the fact that titration of a cold aqueous solution of the compound with standard silver nitrate solution showed that both bromine atoms were ionic, whereas the compound (IV) would clearly have only one ionic bromine atom. This result was further confirmed by the fact that a cold aqueous solution of the compound (III), when treated with aqueous sodium picrate, deposited yellow crystals of the corresponding dipicrate, *i.e.*, of 1,1,4,4-tetramethylethylene-*o*-phenylenediarsonium dipicrate, m.p. 236–238°.

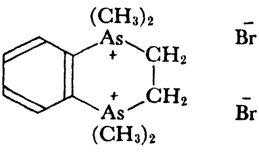
[122a] Glauert and Mann, *unpublished work.*



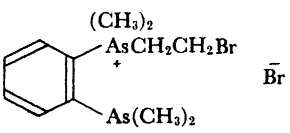
(I)



(II)

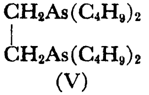


(III)



(IV)

The ready cyclization of *o*-phenylenebis(dimethylarsine), when thus heated with ethylene dibromide, is probably considerably facilitated by the *o*-phenylene group holding the two arsenic atoms firmly in just the position required for this reaction. It is doubtful, for example, if ethylene-1,2-bis(di-*n*-butylarsine) (V), also prepared by Chatt and Mann,[68] would



$$\begin{array}{l} CH_2As(C_4H_9)_2 \\ | \\ CH_2As(C_4H_9)_2 \end{array}$$

(V)

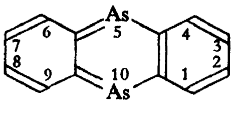
give an equally ready cyclization, for rotation of the arsenic atoms around the ethylene chain might promote the formation of long-chain condensation products rather than a simple cyclized molecule analogous to the compound (III).

Arsanthrene and Its Derivatives

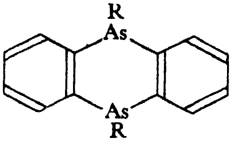
The parent compound in this series is arsanthrene,* with the structure (I), R.I. 1831. The numbering of the ring system adopted in this work is that shown in (I); this is the system adopted in the *Ring Index* and also in *Chemical Abstracts*, and in addition it is in harmony with that used for phenarsazines (p. 80) and phenoxarsines (p. 100). The arsanthrene series resembles the phenarsazine series in that most derivatives

---

* In British nomenclature this word becomes *arsanthren.*



(I)

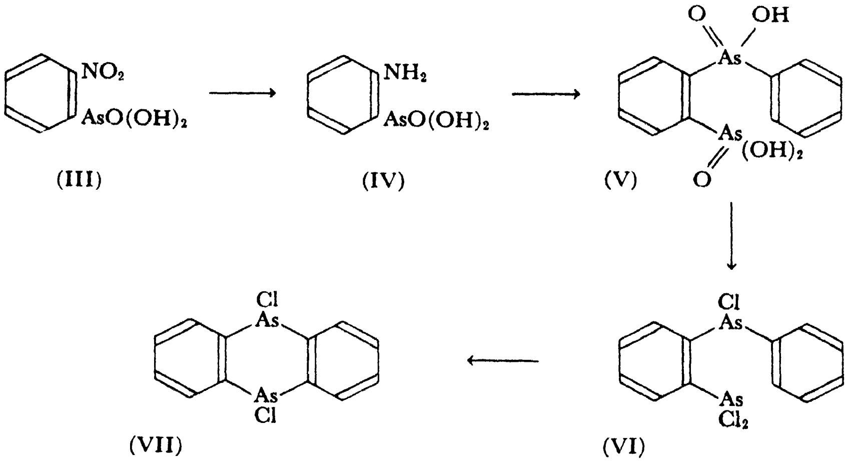


(II)

are of type (II); these are systematically regarded as substitution derivatives of 5,10-dihydroarsanthrene, and are known therefore as 5,10-disubstituted 5,10-dihydroarsanthrenes.

The arsanthrene ring system was first synthesized by Kalb,[66] utilizing the following series of reactions. *o*-Nitraniline was diazotized and converted by the Bart reaction to *o*-nitrophenylarsonic acid (III), which on reduction furnished *o*-aminophenylarsonic acid (IV). The latter was again diazotized and treated with arsenosobenzene, $C_6H_5As:O$, under the usual Bart reaction conditions to give *o*-arsonodiphenylarsinic acid (V). When this acid was mixed with concentrated hydrochloric acid containing a trace of hydriodic acid and then reduced with sulfur dioxide, *o*-dichloroarsino-diphenylchloroarsine (VI), m.p. 153–155°, and 5,10-dichloro-5,10-dihydroarsanthrene, m.p. 182–183°, were isolated from the crude product. The conditions of this reduction and cyclization were subsequently modified by Chatt and Mann[115] so that the yield of the trichloro compound (VI) was reduced and that of the 5,10-dichloro compound (VII) considerably increased. A very interesting by-product which arises at this stage, namely tri-*o*-phenylenediarsine, will be described later.

Kalb investigated other possible routes to avoid this rather tedious synthesis. He attempted to cyclize the arsinic acid (V) by dehydration with sulfuric acid to give arsanthrenic acid (VIII), alternatively named *o*-diphenylenediarsinic acid, but the acid (V) was unaffected by sulfuric acid even at 150°; had this cyclization succeeded, the arsanthrenic acid could have undoubtedly been readily reduced to the 5,10-dichloro compound (VII). He also attempted to condense two molecules of *o*-dibromobenzene with two of arsenic trichloride by means of metallic sodium, *i.e.*, under the normal conditions of a Michaelis condensation, and also

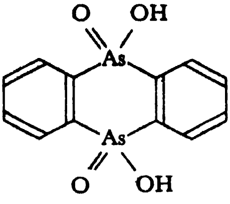


(III) (IV) (V) (VII) (VI)

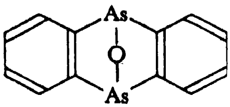
similarly to condense two molecules of *o*-bromophenyldichloroarsine with sodium, in both cases in the vain hope of obtaining the 5,10-dichloro compound (VII). These last two attempts constitute a greater tribute to Kalb's optimism than to his experience and "feel" of synthetic probabilities in the cyclic arsenic field.

When the 5,10-dichloro-5,10-dihydroarsanthrene (VII) was treated with aqueous sodium carbonate, it gave, not the corresponding dihydroxy derivatives, but the so-called "oxide" (IX), or anhydride of the 5,10-dihydroxy derivative, which has already been discussed (p. 75). Reduction of the 5,10-dichloro compound (VII) with zinc and hydrochloric acid, or the oxide (IX) using ethanolic phenylhydrazine, gave the parent arsanthrene (I). This compound is of great interest because it represents one of the very few compounds in which the =As— group does apparently replace the =CH— in an aromatic ring; clearly a compound of constitution (I) could systematically be named 5,10-diarsa-anthracene. Kalb describes this compound as forming orange-yellow plates, which on heating become orange-red at about 170° and greenish-yellow at about

290°, and finally melt at 340°. Unfortunately the molecular weight was not recorded. It will be clear that a compound of constitution (I) would exist as a resonance hybrid, each outer ring being half benzenoid and half quinonoid. Although the existence of resonance is frequently associated with visible color, this is not always the case (*cf.* anthracene), and in view of the above colors it is not absolutely certain that Kalb's compound has the simple structure (I) or whether it is a polymer based on this structure.

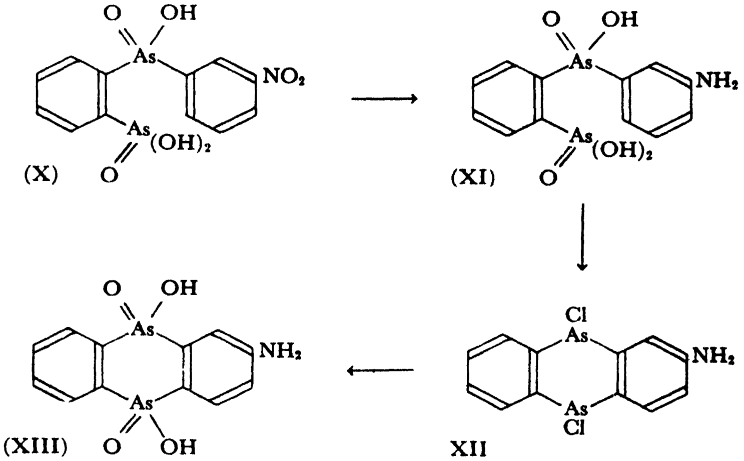


(VIII)



(IX)

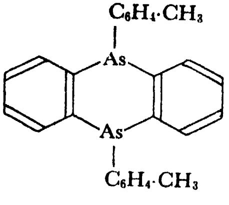
Wieland and Rheinheimer[72] have attempted to nitrate 5,10-dichloro-5,10-dihydroarsanthrene in order subsequently to obtain amino derivatives of arsanthrene. The 5,10-dichloro compound resisted nitration by even energetic nitrating agents, but was converted to the above arsanthrenic acid (VIII), colorless crystals, m.p. above 360°. To overcome this difficulty, the arsinic acid (V) was nitrated to give 2-arsono-3′-nitrodiphenylarsinic acid (X), which on reduction with ferrous hydroxide furnished the 3′-aminoarsinic acid (XI). This compound when reduced under the usual conditions with hydrochloric acid and sulfur dioxide gave 2-amino-5,10-dichloro-5,10-dihydroarsanthrene (XII), the hydrochloride of which formed colorless crystals. Oxidation of this compound gave 2-aminoarsanthrenic acid (XIII) as colorless needles. It should be noted, however, that Wieland and Rheinheimer had no decisive evidence that the nitro group had entered the 3′-position in the arsinic acid (X) and that the amino group had therefore the 3′-position in the acid (XI). Furthermore, assuming that the latter acid has the constitution (XI), it will be seen that on cyclization it could give either the 1-amino- or the 2-amino-5,10-dichloro-5,10-dihydroarsanthrene, although if one can argue by analogy from Roberts and Turner's later work[110] on the cyclization of 3′-chlorodiphenylether-2(dichloroarsine) to the corresponding phenoxarsine (p. 103), the formation of the 2-aminoarsanthrene is the more



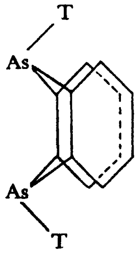
probable. It can be said therefore, that the structures allocated to compounds (X)–(XIII) by Wieland and Rheinheimer are those which are most probable, although not certain.

The stereochemistry of derivatives of 5,10-dichloro-5,10-dihydroarsanthrene (VII) has been investigated by Chatt and Mann.[115] On the basis of the discussion given on p. 108, it will be clear that if the intervalency angle at the arsenic atoms retains its normal value of about 97°, the three rings in the compound (VII) cannot be planar, and that the molecule must be folded about the As—As axis. Arsanthrene derivatives are in one respect more favorable for the study of this phenomenon than the phenoxarsines (p. 110) because in the arsanthrene compounds the folding must be due solely to this arsenic valency angle, whereas in the phenoxarsines it may be influenced to an uncertain degree by the intervalency angle of the oxygen atom.

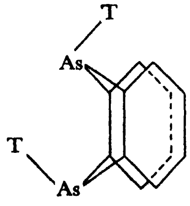
Chatt and Mann, in order to obtain a more stable derivative which in particular would be unaffected by damp air, treated the 5,10-dichloro compound with *p*-tolyl magnesium bromide, and thus obtained 5,10-di-*p*-tolyl-5,10-dihydroarsanthrene (XIV), a compound that formed magnificent colorless crystals. Now if this compound is folded about the As—As axis, it might be expected to exist in three geometrically isomeric forms. The first is represented diagrammatically in (XIVA), in which the symbol T represents the *p*-tolyl group, and in which (as also in the diagrams (XIVB) and (XIVC)) the two arsenic atoms and the two *p*-tolyl groups are represented as being in the plane of the paper, while one *o*-phenylene group projects above the plane of the paper towards the reader, and the second *o*-phenylene group projects below this plane and away from the reader. If the angle between all three valencies of the arsenic atoms remains constant at about 97 °, the first form will have the two tolyl groups in the *cis* position, and lying between the angle subtended by the two *o*-phenylene groups (XIVA); the intervalency angle demands that those



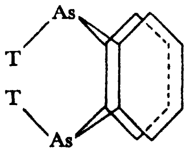
(XIV)



(XIVA)



(XIVB)



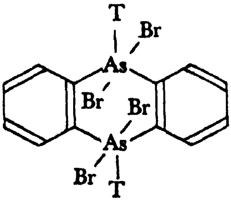
(XIVC)

groups shall project away from the center of the As—As axis as shown. The second form (XIVB) will have the tolyl groups in the *trans* position; now the upper tolyl group is in the same position as before, but the lower group projects towards the center as shown. The diagrams might appear to indicate a third form (XIVC) in which the tolyl groups are in another *cis* position, but both directed inward although away from the *o*-phenylene groups as shown. It will be obvious on consideration, however, that in (XIVC) the two groups T are almost coincident in space, and two groups as large as tolyl groups could not be thus accommodated. Models constructed to scale show the possible existence of the *cis* and *trans* forms (XIVA) and (XIVB), and the impossibility of the existence of a second *cis* form of type (XIVC).

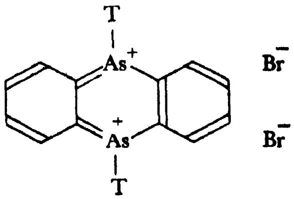
Chatt and Mann found that their 5,10-ditolyl compound (XIV), when initially prepared, formed white crystals, m.p. 133–158°. A slow and delicate process of fractional crystallization ultimately separated this product into the α form, small leaflets, m.p. 178–179°, and the β-form, large bipyramidal leaflets, m.p. 179–181°; a mixture of equal quantities of the two forms melted at 144–158°. Each isomer showed the correct molecular weight in boiling acetone. The two forms were moreover surprisingly stable, for each isomer could be kept in the molten condition at 190° for 10 minutes without any indication either of conversion in the other form, or of chemical decomposition. It is not of course known which of these forms has the *cis* configuration (XIVA) and which has the *trans* configuration (XIVB).

The difference between these isomers extended also to their monomethiodides. Each monomethiodide had m.p. 178–179°, but a mixture of equal quantities of the two compounds melted at 167–175°. The α-monomethiodide crystallized from ethanol with one molecule of ethanol of crystallization, and from water in the anhydrous condition; the β-monomethiodide crystallized from ethanol in the pure solvent-free condition, but from water as the monohydrate. Neither salt would form a dimethiodide. Since there was no steric reason for this inability, it was attributed to the strong positive charge on the arsonium ion in the monomethiodide exerting a powerful inductive effect toward this ion. This effect would be readily transmitted through the neighboring *o*-phenylene groups, and consequently there would be a considerable electronic drag away from the second arsenic atom. This drag would tend very largely to inactivate the lone pair of electrons on this atom which are normally involved in quaternary salt formation. This phenomenon of inductive deactivation, in both this and many other compounds, has been discussed in some detail by Mann and Watson.[123]

It is noteworthy that both the α and β forms of the 5,10-di-*p*-tolyl-5,10-dihydroarsanthrene when treated with bromine gave the same tetrabromide (XV), the identity of which as a single compound was further confirmed by hydrolysis to the highly crystalline tetrahydroxide. This loss of isomeric difference in the tetrabromide is to be expected. It will be recalled that Wells[54] has found that in trimethylstibine dihalides, the antimony atom is in the center of an equilateral triangle having the methyl groups at its apices, and having the halogen atoms lying at equal distances above and below the antimony atom on an axis perpendicular to the plane of the triangle [see (XIV), page 67]. It follows that in these compounds, the C—Sb—C angle is 120°. If Wells' results apply also to tertiary arsine dihalides, it follows that the C—As—C angle in the ring in the tetrabromide (XV) is also 120°; consequently the three rings now become uniplanar, and no basis for geometric isomerism exists.



(XV)



(XVI)

It should be added that when the tetrabromide was reduced back to the original 5,10-ditolyl derivative (XIV), an x-ray examination revealed the presence of only two isomers identical with those already obtained. This confirms the nonexistence of a third isomer, for had this existed, it might well have been formed with the others by this method.

---

[123] Mann and Watson, *J. Org. Chem.*, **13**, 502 (1948).

When the tetrabromide was treated with an excess of sodium sulfide, it gave elementary sulfur and 5,10-di-*p*-tolyl-5,10-dihydroarsanthrene monosulfide. The latter could not be converted to a disulfide or to a monosulfide monomethiodide, undoubtedly because even the weak positive pole on the $\overset{+}{\text{As}}\text{—}\overset{-}{\text{S}}$ group was sufficient to inactivate the second arsenic atom.

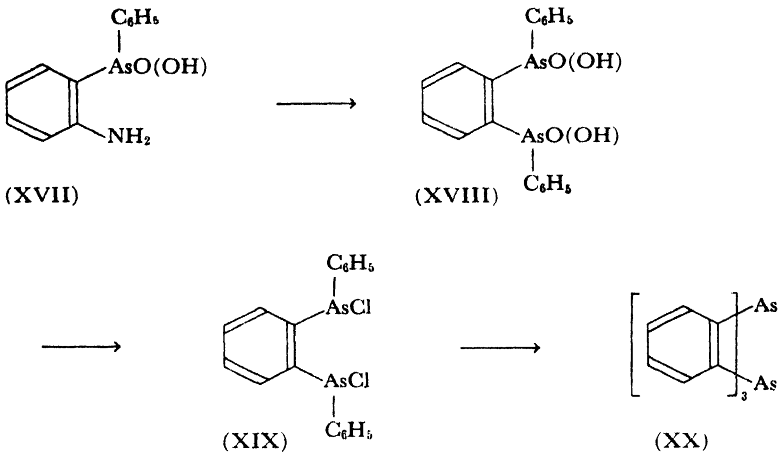
When, however, the tetrabromide was treated with hydrogen sulfide, it gave the above monosulfide and also 5,10-di-*p*-tolyl-5,10-dihydroarsanthrene dibromide. The properties of this compound indicated that the two bromine atoms were probably not linked covalently to one arsenic atom, but that the compound was a salt of structure (XVI). The evidence for the ionic structure is as follows. (*1*) The dibromide is soluble in hot water, ethanol, and other polar solvents, but not in ether or benzene. These are the properties of an electrovalent, and not a covalent compound. (*2*) The dibromide can be recrystallized unchanged from hot aqueous ethanol, whereas most tertiary arsine dibromides, R_3AsBr_2, give the corresponding hydroxy bromide, $R_3As(OH)Br$, in these circumstances. (*3*) It reacts very slowly with hydrogen sulfide to give the above monosulfide, whereas most dibromides of type R_3AsBr_2 readily give the sulfide R_3AsS under these conditions. (*4*) Its high melting point, 298–300°, is more in the region expected of a salt rather than a true covalent compound. In view of the considerable stability of the dibromide, it should be noted that if it had the ionic structure (XVI), it would of course exist as a resonance hybrid, which would enhance its stability.

Tri-o-phenylenediarsine

This compound (XX), which is clearly related to arsanthrene, was first synthesized and recognized by McCleland and Whitworth.[124] These workers diazotized *o*-aminodiphenylarsinic acid (XVII) and then coupled the product with arsenosobenzene, $C_6H_5As{:}O$, to give phenylene-1,2-diphenylarsinic acid (XVIII). This was treated with phosphorus trichloride, whereby it presumably underwent reduction to phenylene-1,2-diphenylchloroarsine (XIX); the latter was not isolated, however, for the crude product was heated under reduced pressure, when hydrogen chloride was evolved and colorless crystals of tri-*o*-phenylenediarsine (XX) sublimed onto the upper and cooler portions of the flask. A second crop was obtained by extracting the charred residue in the flask with boiling benzene.

---

[124] McCleland and Whitworth, *J. Chem. Soc.*, **1927**, 2753.

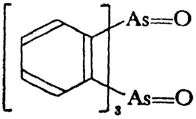


(XVII) (XVIII) (XIX) (XX)

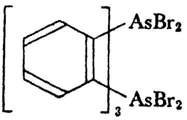
McCleland and Whitworth also showed that, although "arsanthrene oxide" (IX) would distil at 15 mm. pressure without appreciable decomposition, yet when heated in a current of carbon dioxide at pressures only slightly less than atmospheric, considerable decomposition occurred with the formation of arsenious oxide and tri-*o*-phenylenediarsine.

The diarsine (XX) is also formed as a by-product in Kalb's conversion of *o*-arsonodiphenylarsinic acid (V) to 5,10-dichloro-5,10-dihydroarsanthrene (VII).[22] The modification of this process developed by Chatt and Mann[115] considerably decreases the yield of the intermediate *o*-dichloroarsinodiphenylchloroarsine (VI), but nearly doubles that of the tri-*o*-phenylenediarsine (XX).

The diarsine (XX) forms almost colorless crystals, m.p. 295–296°. When boiled with nitric acid it gives the crystalline dioxide (XXXI); the absence of nitration in these circumstances recalls the resistance of 5,10-dichloro-5,10-dihydroarsanthrene (VII) to nitration. The diarsine also readily adds on bromine to give the tetrabromide (XXII), orange-red crystals, m.p. 255–256°. This tetrabromide is readily hydrolyzed, even by water, to give the dioxide (XXI). When heated under reduced pressure, it undergoes considerable decomposition, with the formation of *o*-dibromobenzene and 5,10-dibromo-5,10-dihydroarsanthrene.



(XXI)



(XXII)

It is noteworthy that the diarsine was unaffected by prolonged heating with methyl iodide in a sealed tube at 50–60 °. This is curious because it might have been expected that the disposition of the three valencies of each arsenic atom in the diarsine (XX) would have allowed a reasonably ready ingress of a methyl group as each arsenic atom became a tetrahedral arsonium ion, whereas the formation of a dibromide might have put considerable strain on these three valencies. The diarsine and its derivatives clearly deserve considerably greater attention and study.

Seven-Membered Ring Systems Containing Carbon and Two Arsenic Atoms

o-Phenylenetrimethylenediarsine

It has been shown by Glauert and Mann[122a] that derivatives containing this ring system can readily be made by a method precisely analogous to that which these authors have employed to prepare derivatives of ethylene-*o*-phenylenediarsine (see p. 116).

When a mixture of equimolecular quantities of *o*-phenylenebis(dimethylarsine) and trimethylene dibromide is heated, combination readily occurs with the formation of the highly crystalline dimethobromide of As,As-dimethyl-*o*-phenylenetrimethylenediarsine, m.p. 258°. Evidence that cyclization has occurred in the reaction and that both arsenic atoms are members of a seven-membered ring is proved by the fact that both bromine atoms are now ionic, *i.e.*, the compound is a diarsonium salt. This is confirmed by the fact that a cold aqueous solution of the dibromide, when poured into an excess of sodium picrate solution, deposits the corresponding dimethopicrate of As,As-dimethyl-*o*-phenylenetrimethylenediarsine, m.p. 260°.

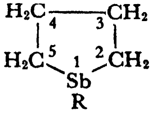
CHAPTER III

Heterocyclic Derivatives of Antimony

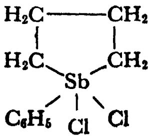
Five-Membered Ring Systems Containing Only Carbon and Antimony

Cyclotetramethylenestibines

These compounds have the general formula (I), R.I. 116, and hence are the antimony analogs of *N*-substituted pyrrolidines. At present, however, apparently only one tertiary stibine in this series is known. Grüttner and Krause[125] have shown that 1-phenylcyclotetramethylenestibine (I, R = C_6H_5) can be prepared by the same method they employed for the synthesis of the phosphorus and arsenic analogs, *i.e.*, the Grignard reagent prepared from 1,4-dibromobutane, $(\cdot CH_2 \cdot CH_2MgBr)_2$, being treated with phenyldichlorostibine, $C_6H_5SbCl_2$, in cold ether under an atmosphere of hydrogen. The tertiary stibine was thus obtained as a colorless oily liquid, b.p. 156–158°/20–20 mm., having an unpleasant odor, and readily becoming cloudy by oxidation on exposure to air. When a solution of the stibine in carbon tetrachloride was treated with chlorine, the 1-phenylcyclotetramethylenestibine dichloride (II) was formed; when recrystal-



(I)



(II)

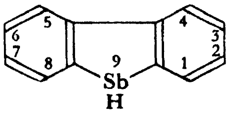
---

[125] Grüttner and Krause, *Ber.*, **49**, 442 (1916).

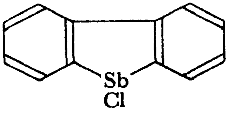
lized from carbon tetrachloride it formed white crystals, m.p. 150°. The stibine dibromide, similarly obtained, also formed white crystals, m.p. 149°.

Stibinafluorenes

These compounds can all be regarded as derivatives of the unknown compound (I), R.I. 1747, in which the hydrogen atom linked to the antimony is replaced by halogen, alkyl, aryl, or other groups. No satisfactory name has hitherto been devised for compounds having this ring system. Morgan and Davies,[126] who first prepared compounds of this class from 2-aminobiphenyl, revived a term originally used by Hofmann[127] for the three isomeric monoaminobiphenyls and termed them "xenylamines"; consequently, 2-aminobiphenyl was termed *o*-xenylamine. On this basis, the monovalent biphenylyl radicals, $C_6H_5 \cdot C_6H_4$— (three in number), were termed the "xenyl" radicals, and the divalent biphenylene radicals, —$C_6H_4 \cdot C_6H_4$— or $C_6H_5 \cdot C_6H_3 =$ (twelve in number) were termed the "xenylene" radicals. Since, for example, the cyclic chlorostibine (II) was obtained from *o*-xenylamine, it was termed "xenylenestibine chloride." Although in the 4th edition of Beilstein's *Handbuch der Organischen Chemie*, the term "xenyl" is given as an alternative synonym for "biphenylyl" and "diphenylyl," its use has never been generally adopted and to many chemists its meaning is obscure. The term "xenylenestibine chloride" for (II) is therefore also undesirable.



(I)



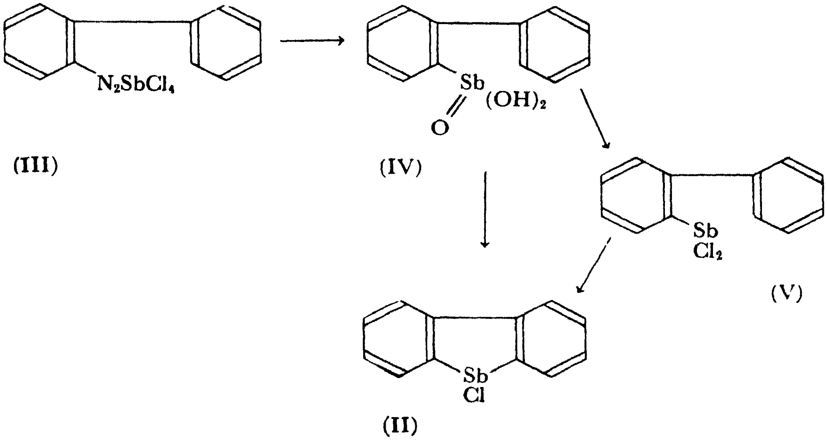
(II)

The corresponding arsenic derivatives (p. 36) were termed "arsafluorenes" to indicate that they represented fluorene with the —CH_2— group replaced by —AsR—, and consequently it is now proposed to call the compound (I) "stibinafluorene" and to number the ring atoms as shown, in harmony with the system used for the arsafluorenes.

---

[126] Morgan and Davies, *Proc. Roy. Soc. London*, **A127**, 1 (1930).
[127] Hofmann, *Proc. Roy. Soc.*, **A12**, 393, 576 (1862–1863).

In Morgan and Davies' synthesis,[126] 2-aminobiphenyl was first diazotized in the presence of hydrochloric acid, and the cold solution was then treated with a solution of antimony trioxide in concentrated hydrochloric acid (compare Rose[128]), whereby pale yellow crystals of biphenylyl-2-diazonium antimony tetrachloride (III) were obtained. A suspension of these crystals in ice water was first stirred with aqueous sodium hydroxide solution until decomposition of the diazonium salt was complete and evolution of nitrogen had ceased, and was then warmed with dilute hydrochloric acid to precipitate the biphenylyl-2-stibonic acid (IV); the latter, after purification from inorganic antimony compounds, was ultimately obtained as colorless crystals by recrystallization from ethanol.



When a solution of the stibonic acid (IV) in methanolic hydrochloric acid containing a trace of potassium iodide was treated at room temperature with sulfur dioxide, ready reduction occurred to form biphenylyl-2-(dichlorostibine) (V), colorless needles, m.p. 76°. This compound was further characterized by treatment with an acetone solution of sodium iodide, whereby the corresponding 2-(di-iodostibine) was obtained as dark yellow needles, m.p. 95–96°.

The 9-chlorostibinafluorene (II) was obtained by cyclization either of the dichlorostibine (V) or of the stibonic acid (IV). When the dichlorostibine (V) was heated at 100°/25 mm. pressure, hydrogen chloride was lost and the 9-chloro derivative (II) obtained as greenish white crystals, m.p. 209°. More satisfactory results were obtained, however, when the stibonic acid (IV) was dissolved in concentrated sulfuric acid, and the solution warmed at 100° for 10 minutes and then poured into much cold water. The precipitated material was dissolved in methanolic hydrochloric acid and reduced as before with sulfur dioxide, yielding the 9-chlorostibinafluorene. This compound was also characterized by treatment with sodium iodide in acetone solution, giving lemon-yellow needles of 9-iodostibinafluorene, m.p. 222°.

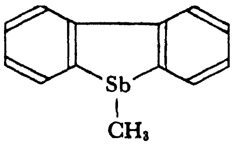
---

[128] Rose, *J. Chem. Soc.*, **101**, 1037 (1912).

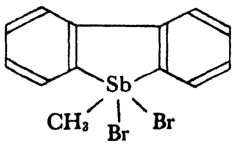
It should be noted that when the sulfur dioxide reductions cited above are carried out, care has to be taken to ensure that an excess of the dioxide is not used, otherwise the reduction proceeds too far, with the separation of elementary antimony. In arsenic compounds this extreme reduction to elementary arsenic is apparently never encountered.

When the 9-chloro compound was hydrolyzed by being poured in acetone solution into an excess of dilute aqueous ammonia, the "oxide," $C_{12}H_8{:}Sb{\cdot}O{\cdot}Sb{:}C_{12}H_8$, was obtained as yellowish-white crystals, m.p. 177–179°. This compound is of course systematically the anhydride of 9-hydroxystibinafluorene.

An ethereal suspension of 9-iodostibinafluorene, when treated with methyl magnesium iodide, gave the tertiary stibine, 9-methylstibinafluorene (VI), as colorless crystals, m.p. 57°. It is noteworthy that this stibine would not combine with methyl iodide, although it united readily with one molecular equivalent of bromine to give the stibine dibromide (VII), a pale yellow microcrystalline powder, m.p. 207°.

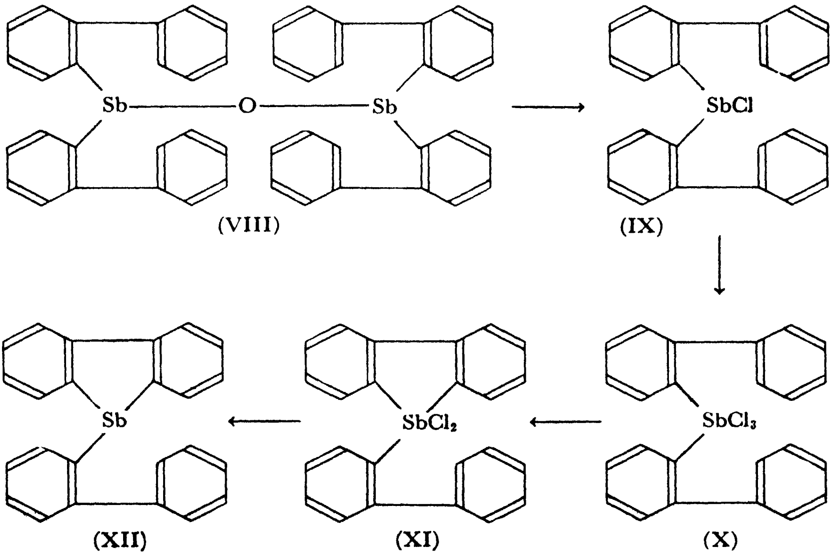


(VI)



(VII)

Certain properties of biphenylyl-2-(dichlorostibine) (V) and its derivatives deserve discussion, because they illustrate the extraordinary ease with which organic derivatives of antimony may in certain cases undergo dismutation, and they also provide another route for cyclization to the stibinafluorene ring system. Morgan and Davies[126] found that when the dichlorostibine (V) was digested with warm dilute aqueous sodium hydroxide, it underwent dismutation with the formation of antimony trioxide and the "oxide" (VIII). The latter is clearly the anhydride of bis(2-biphenylyl)hydroxystibine, $(C_6H_5{\cdot}C_6H_4)_2Sb(OH)$, and this is confirmed by the fact that on treatment with hot ethanolic hydrochloric acid it gives bis(2-biphenylyl)monochlorostibine (IX), colorless crystals, m.p. 125.5°, which can be converted in the usual way to the corresponding monoiodostibine, yellow crystals, m.p. 156–157°. The anhydride (VIII) is in fact best purified by this conversion to the monochlorostibine (IX), for when an acetone solution of the latter is added to a large volume of dilute aqueous ammonia, the pure anhydride (VIII) can be readily isolated as large colorless needles, m.p. 157°.



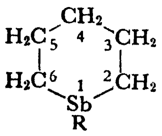
(VIII) (IX) (X) (XI) (XII)

The bis(2-biphenylyl)monochlorostibine (IX) in chloroform solution readily combined with one molecular equivalent of chlorine to give the trichloro derivative (X), colorless needles, m.p. 177°, and this compound, when heated at 50°/20 mm. underwent cyclization with loss of hydrogen chloride to form 9-(2-biphenylyl)stibinafluorene dichloride (XI), colorless crystals, m.p. 212°. This product could be reduced to the tertiary stibine by boiling in ethanolic suspension with zinc dust for 2 hours, and the 9-(2-biphenylyl)stibinafluorene (XII) obtained as colorless needles, m.p. 106–107°.

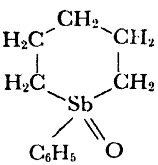
Six-Membered Ring Systems Containing Only Carbon and Antimony

Cyclopentamethylenestibines

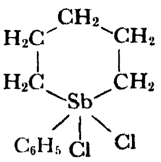
These tertiary stibines, which are of general formula (I), R.I 210, and hence are the antimony analogs of the *N*-substituted piperidines, are prepared by a method precisely similar to that by which their phosphorus and arsenic analogs have been obtained. Grüttner and Wiernik[129] have prepared 1-phenylcyclopentamethylenestibine (I, R = C_6H_5) by the interaction of the Grignard reagent obtained from 1,5-dibromopentane, *i.e.*, $CH_2(CH_2CH_2MgBr)_2$, and phenyldichlorostibine, $C_6H_5SbCl_2$, working in an inert atmosphere. This stibine forms a colorless, rather oily liquid, b.p. 169–171°/18–20 mm., having a faint unpleasant odor. Atmospheric oxidation gives the stibine oxide (II), a colorless powder which does not melt below 280°, while chlorine, when passed into a solution of the stibine in carbon tetrachloride, gives the stibine dichloride (III); this compound can be recrystallized from ethanol containing approximately 10% of concentrated aqueous hydrochloric acid, and obtained as colorless crystals, m.p. 141–142°. In contrast to these two addition reactions, the tertiary



(I)



(II)



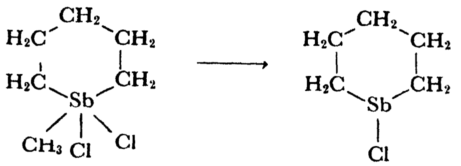
(III)

---

[129] Grüttner and Wiernik, *Ber.*, **48**, 1484 (1915).

stibine does not give a mercuric chloride addition product, and when heated with boiling ethyl iodide for 3 hours was unaffected. Its reaction with methyl iodide has apparently not been recorded.

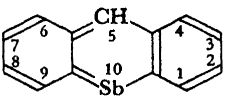
1-Methylcyclopentamethylenestibine (I, R = CH_3) has been prepared much later by Steinkopf, Schubert, and Roche,[130] by the interaction of the Grignard reagent prepared from 1,5-dichloropentane and methyldichlorostibine. It is a colorless liquid, b.p. 73–73.5°/17 mm., with an unpleasant odor. When treated in petroleum solution with chlorine it forms the stibine dichloride (IV), which, in turn, on being heated to 160–185°, loses methyl chloride with the formation of 1-chlorocyclopentamethylenestibine (V), a liquid having b.p. 110–111°/13 mm. This decomposition of the dichloride (IV) is precisely similar to that shown by 1-methylcyclopentamethylenearsine dichloride (p. 38) and is indeed a reaction of frequent occurrence with tertiary methylarsine dichlorides (*cf.* p. 26).



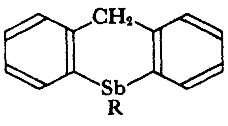
(IV) (V)

Stibacridines

The term stibacridine is applied to the unknown compound (I), R.I. 2025, *i.e.*, to the compound which would be obtained if the nitrogen atom in acridine could be replaced by an antimony atom. The term stib-



(I)



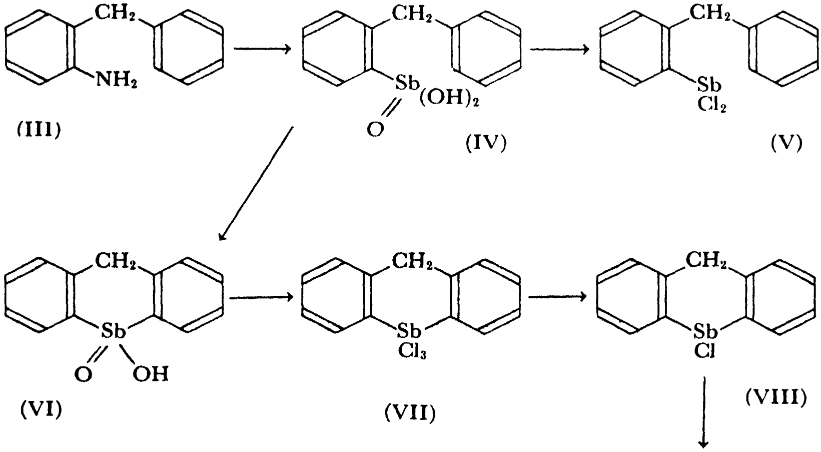
(II)

---

[130] Steinkopf, Schubert, and Roch, *Ber.*, **65**, 409 (1932).

acridine, although unsystematic, has become sufficiently well recognized to be retained, and the more accurate name 10-stibina-anthracene has therefore not been adopted in this monograph; it will be remembered that on similar grounds the term arsacridine was retained for corresponding arsenic compounds (pages 3, 49). All known compounds in the stibacridine series are, however, derivatives of 5,10-dihydrostibacridine, and are indeed 10-substituted 5,10-dihydrostibacridine derivatives of type (II).

Compounds of the latter class have been synthesized by Morgan and Davies[131] by a series of reactions closely parallel to those used earlier by Gump and Stoltzenberg[132] in their original synthesis of arsacridine derivatives (p. 50). For this purpose, 2-aminodiphenylmethane (III) in



(III) (IV) (V)

(VI) (VII) (VIII)

(IX) $C_{13}H_{10}:Sb\cdot O\cdot Sb:C_{13}H_{10}$

hydrochloric acid solution was first diazotized by the addition of sodium nitrite and then treated with a solution of antimony trioxide in hydrochloric acid and with glycerol to check subsequent foaming. The agitated ice-cold mixture was then treated with aqueous 5 *N* sodium hydroxide solution until evolution of nitrogen was complete. Colored impurities and free antimony oxide were first precipitated by saturating the solution with carbon dioxide, and the diphenylmethane-2-stibonic acid (IV) then precipitated with hydrochloric acid. The stibonic acid was thus obtained as a colorless amorphous powder, sufficiently pure for subsequent synthetic purposes; the pure acid was obtained by recrystallization from an ethanol–methylene dichloride mixture and obtained as small pale-colored needles, which were only slowly soluble in hot dilute aqueous sodium hydroxide.

---

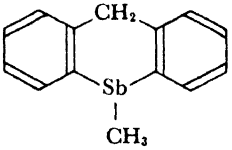
[131] Morgan and Davies, *Proc. Roy. Soc. London*, **A143**, 38 (1933).
[132] Gump and Stoltzenberg, *J. Am. Chem. Soc.*, **53**, 1428 (1931).

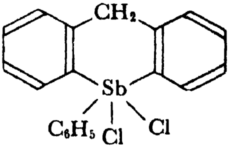
A number of derivatives of this acid were prepared. For example, when a mixture of the acid with methanolic hydrochloric acid was reduced in the usual way with sulfur dioxide, the diphenylmethane-2-(dichlorostibine) (V) was obtained as colorless needles, m.p. 129–130°. This compound in acetone solution when treated with sodium iodide readily gave the 2-(di-iodostibine), golden-yellow crystals, m.p. 95°. When a similar solution of the dichloro compound was poured into ice-cold dilute aqueous ammonia, diphenylmethane-2-(stibine oxide), $C_6H_5 \cdot CH_2 \cdot C_6H_4 \cdot SbO$, was obtained as a microcrystalline powder, m.p. 82–83°, which when treated with hydrobromic acid gave the 2-(dibromostibine), colorless plates, m.p. 221°.

Attempts to cyclize the dichloro compound (V) by heating it in a vacuum and so to obtain 10-chloro-5,10-dihydrostibacridine (VIII) failed. Attempts to cyclize the stibonic acid (IV) by means of hot concentrated sulfuric acid also failed. Ultimately, cyclization was achieved by mixing the stibonic acid (IV) with a considerable quantity of acetic anhydride containing 3.4% (by volume) of sulfuric acid, and then heating at 100° for 3 hours. When the mixture was poured into warm water, the crude stibacridinic acid (VI) was precipitated as a pale brown powder. This acid was washed, dried, and then treated with ice-cold hydrochloric acid, whereby the trichloride (VII) was obtained. The latter was dissolved in methanol, reduced with sulfur dioxide and finally treated with hydrochloric acid, the 10-chloro-5,10-dihydrostibacridine (VIII) being finally isolated as colorless needles, m.p. 105°.

The 10-chloro derivative was characterized by direct conversion to the 10-iodo compound, yellow needles, m.p. 160–162°, and by hydrolysis with dilute aqueous ammonia to the anhydride (IX) of the 10-hydroxy compound; the latter, in turn, when treated with hydrobromic acid, gave the 10-bromo derivative, colorless crystals, m.p. 112°.

When the 10-iodo derivative in ethereal solution was treated with methyl magnesium iodide, the 10-methyl-5,10-dihydrostibacridine (X) was obtained as colorless crystals, m.p. 101°. This tertiary stibine, when treated in methylene dichloride solution with chlorine, gave the tertiary stibine dichloride, $C_{13}H_{10}:Sb(CH_3)Cl_2$, as colorless crystals which melted at 177–178° with evolution of gas. A similar addition of iodine gave a crude di-iodide but all attempts to recrystallize this compound caused decomposition with the formation of methyl iodide and of 10-iodo-5,10-dihydrostibacridine. The crude dibromide decomposed similarly.

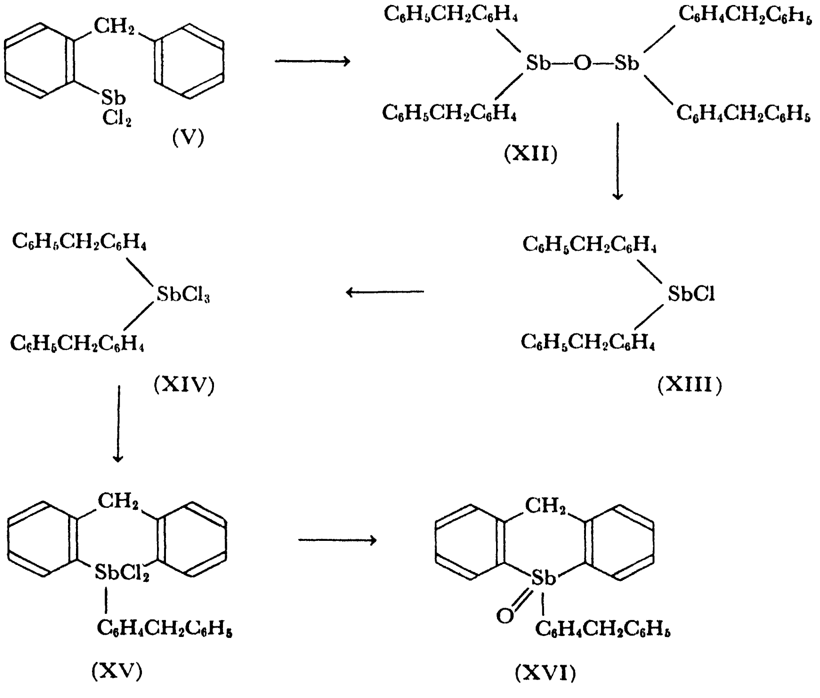

(X)


(XI)

Attempts were made to prepare the 10-phenyl derivative by treating the 10-iodo compound with phenyl magnesium bromide, but the crude product underwent such ready oxidation that it was stabilized by addition of chlorine, and the 10-phenyl-5,10-dihydrostibacridine dichloride (XI) isolated as colorless crystals, m.p. 221–223°.

Diphenylmethane-2(dichlorostibine) (V) showed the same ready dismutation under the influence of alkalis as that shown by biphenylyl-2-(dichlorostibine) (p. 133), and a similar series of derivatives was obtained. Thus, when the 2-(dichlorostibine) (V) in acetone solution was added to an excess of dilute aqueous ammonia, antimony oxide was split off and the anhydride (XII) of bis(2-diphenylmethane)hydroxystibine was formed as colorless needles, m.p. 117°. This anhydride, when treated in acetone solution with ice-cold concentrated hydrochloric acid, gave bis(2-diphenylmethane)monochlorostibine (XIII), needles, m.p. 87.5°. Addition of chlorine to the latter compound then furnished the trichlorostibine (XIV), colorless plates, m.p. 129°, which when heated at 150–180° at

18–20 mm. underwent slow cyclization with loss of hydrogen chloride and the formation of 10-(2-diphenylmethane)-5,10-dihydrostibacridine dichloride (XV). It was difficult to purify the latter directly and it was therefore hydrolyzed to the corresponding stibacridine oxide (XVI), which after purification and treatment with hydrochloric acid gave the pure dichloride (XV) as a microcrystalline powder, m.p. 220–224° (decomp.). No attempts to reduce this dichloride to the tertiary stibine are recorded.



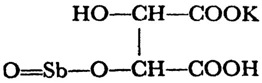
(V) (XII) (XIII) (XIV) (XV) (XVI)

Five-Membered Ring Systems Containing Carbon, Antimony, and Oxygen

Potassium Antimonyl Tartrate (Tartar Emetic)

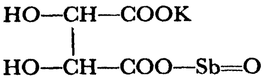
Potassium antimonyl tartrate, or tartar emetic, $KSbC_4H_4O_7 \cdot \frac{1}{2}H_2O$, is a compound whose preparation and general properties are too well known to require detailed description. It is obtained by boiling antimony trioxide with an aqueous solution of potassium hydrogen tartrate, and can be recrystallized readily from water. Its solubility in water is 8.3 g./100 cc. at 25° and 33 g./100 cc. at 100°. Its aqueous solution does not show the normal reactions of the antimony (Sb^{3+}) ion. Other salts, such as sodium antimonyl tartrate, are prepared in the same way and have similar properties.

Various structural formulas have been put forward for tartar emetic, and it is still not certain, although it is probable, that the compound possesses a heterocyclic antimony ring. Among these suggested formulas are the open-chain structures (I) and (II), and the cyclic structures (III) and (IV). The improbable structure (V) has also been advanced.



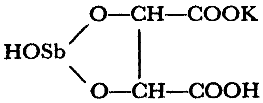
$$\begin{array}{r} \text{HO—CH—COOK} \\ \mid \quad\quad\;\; \\ \text{O=Sb—O—CH—COOH} \end{array}$$

(I)

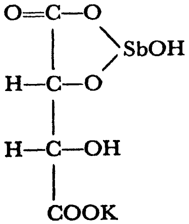


$$\begin{array}{l} \text{HO—CH—COOK} \\ \quad\;\; \mid \\ \text{HO—CH—COO—Sb=O} \end{array}$$

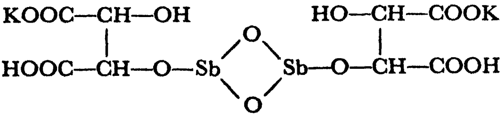
(II)



(III)

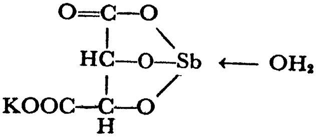


(IV)



(V)

The structure of potassium (and other metallic) antimonyl tartrates has been reinvestigated by Reihlen and Hegel,[133] who suggest the structure (VI), in which a molecule of water is coordinated to the antimony,* and in which the half-molecule of water in the formula $KSbC_4H_4O_7 . \frac{1}{2}H_2O$ is regarded as true water of crystallization and hence can be disregarded. In support of the latter point, they show that barium antimonyl tartrate when treated with 2-phenylethylamine sulfate, gives the crystalline salt $C_6H_5C_2H_4NH_2,HSbC_4H_4O_7$, and that 2-*p*-nitrophenylethylamine gives a similar salt. Since both these salts are devoid of the extra half-molecule of water present in the potassium salt, this half-molecule must be true water of crystallization. The existence of only one free carboxylic acid group in the antimonyl tartrates is shown by the fact that when silver antimonyl tartrate is boiled with an excess of an alkyl iodide, only the monoalkyl antimonyl tartrate ester is formed.[134]



(VI)

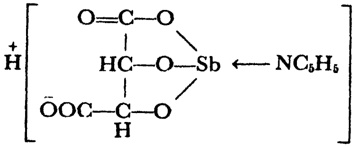
A moderate quantity of evidence for the structure (VI) is put forward, but it is not completely convincing. The authors show that a molecular model indicates that the structure (VI), when composed of *d*-tartaric units, would be strainless. Attempts to prepare an analogous salt from the potassium hydrogen salt of *meso*-tartaric acid failed, however. Furthermore, when barium antimonyl tartrate was treated with pyridine sulfate, a pyridine antimonyl tartrate was isolated. When this compound was dissolved in water, its optical rotation increased rapidly on dilution to that of an equimolecular solution of tartar emetic. Consequently, the solid

---

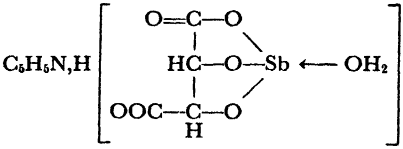
* Reihlen and Hegel state that this molecule of water is linked to the antimony atom by a "residual valence," which they indicate by a dotted line. By this valence they presumably mean a coordinate link; if so, it must be in the direction shown in (VI) since the oxygen atom could not increase the number of its electrons, whereas this process is not impossible for the antimony atom (*cf.*, the compounds $SbCl_5$ and $C_6H_5SbCl_4$, etc.). But there is some ambiguity regarding the precise nature of the bonds intended by these authors in the formulas (IX) and (X).

[133] Reihlen and Hegel, *Ann.*, **487**, 213 (1931).

[134] Christiansen and Norton, *J. Am. Chem. Soc.*, **47**, 876 (1925).



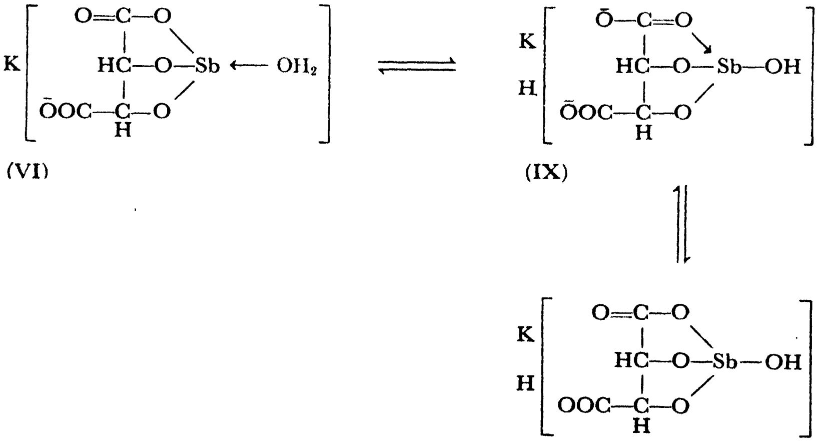
(VII)



(VIII)

compound was considered to be an acid of constitution (VII), which in solution reverted to the salt (VIII). The formation of the compound (VII), as the coordinated pyridine analog of the true tartar emetic (VI), and its ready conversion to the tartar emetic structure in (VIII), was considered to support the structure given in (VI).

Reihlen and Hegel[133] point out that in aqueous solution potassium antimonyl tartrate is only slightly hydrolyzed (presumably to potassium hydrogen tartrate and antimony trihydroxide), but that the solution has an acid reaction; for example, a 0.2N aqueous solution at 16 ° has pH 4.2. This acid reaction is attributed to "intramolecular hydrolysis" which they interpret by the following series of changes:



(VI)

(IX)

(X)

There is no decisive evidence for these changes, and electronically they are unsatisfactory.

Bodendorf[135] considers that Reihlen and Hegel's formula (VI) is supported apparently both by chemical analogies and by the therapeutic properties of tartar emetic itself.

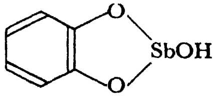
An x-ray crystal analysis of tartar emetic or of any other of the metallic antimonyl tartrates might provide much more accurate and decisive knowledge of the structure of these compounds. For an account of the therapeutic application of tartar emetic, see Schubert[136] and also Bang and Hairston.[137]

Derivatives of Pyrocatechol and Other 1,2-Dihydric Phenols

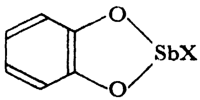
Antimony combines with pyrocatechol and other 1,2-dihydric phenols to give cyclic derivatives more readily than does arsenic. These compounds can be conveniently divided into three classes, according to whether the antimony is linked to one, two, or three units of the phenol; these three classes will be considered in turn.

Class I

The compound (I) is the simplest example in this class. It is frequently termed pyrocatechyl antimonite; systematically, however, it should be regarded as an ester of pyrocatechol and stibinous acid, $(HO)_3Sb$, and hence termed *o*-phenylene hydrogen stibinate. Causse[138] has shown that when a "neutral" aqueous solution of antimony trichloride, *i.e.*, a solution of antimony trioxide in hydrochloric acid to which sodium carbonate has subsequently been added, is run into a 10% aqueous solution of pyrocatechol saturated with sodium chloride and maintained at 50°, the mixture on cooling deposits the crystalline hydroxy compound (I). On heating, this compound apparently decomposes without melting. It is insoluble in all the usual neutral solvents, and is decomposed by boiling water or by hydrogen sulfide.



(I)



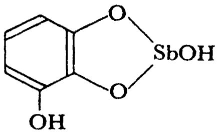
(II)

---

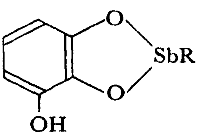
[135] Bodendorf, *Pharm. Presse*, **38**, Wiss.-prakt. Heft 8 (1933).
[136] Schubert, *Am. J. Trop. Med.*, **28**, 121 (1948).
[137] Bang and Hairston, *Am. J. Hyg.*, **44**, 348 (1946).
[138] Causse, *Compt. rend.*, **114**, 1072 (1892).

Causse[139] subsequently showed that an aqueous solution of antimony trichloride, *i.e.*, a solution containing free hydrochloric acid instead of sodium chloride, reacted with an aqueous solution of pyrocatechol to give pyrocatechylchlorostibine or *o*-phenylene chlorostibonite (II, X = Cl), crystalline plates which were also insoluble in the usual solvents. This compound reacted vigorously with acetic anhydride to form pyrocatechyl diacetate, $C_6H_4(O{\cdot}OCCH_3)_2$. The bromo derivative (II, X = Br) was obtained using antimony tribromide, or alternatively by treating the hydroxy compound (I) cautiously with hydrobromic acid. To obtain the iodo derivative (II, X = I), a dilute aqueous solution of hydriodic acid was first saturated with potassium iodide and then with antimony trioxide, and some pyrocatechol was finally added. This solution was then poured into an aqueous solution of pyrocatechol at 40–50°, and, on cooling, the iodo derivative crystallized out. The fluoro and the hydrogen oxalato derivatives were also prepared.

Causse and Bayard[140] showed that the method employed to prepare the compound (I) could also be used to obtain the corresponding pyrogallol derivative (III). When solutions of pyrogallol and of antimony trichloride, each in saturated brine, were mixed, a white flocculent precipitate was formed, and after several hours it changed to small dense crystals. Later, Causse[141] prepared this compound by the action of pyrogallol on a solution of antimony trioxide in aqueous tartaric acid; this method became widely used subsequently. Causse and Bayard[140] found that the compound (III) was insoluble in water and the usual neutral organic solvents: it dissolved in the strong mineral acids, but with complete



(III)

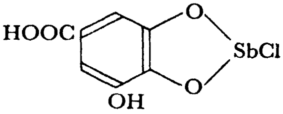


(IV)

---

[139] Causse, *Compt. rend.*, **125**, 954 (1897).
[140] Causse and Bayard, *Compt. rend.*, **115**, 507 (1892).
[141] Causse, *Ann. chim. et phys.* [VII], **14**, 526 (1898).

decomposition. A number of simple derivatives of the compound (III) were prepared.[141] Thus, the chloro derivative (IV, R = Cl) was best prepared by the action of antimony trichloride on a solution of pyrogallol in methanol. The bromo derivative was similarly prepared and could be crystallized from dilute hydrobromic acid. The iodo, fluoro, and hydrogen oxalato derivatives were also prepared. All these compounds formed colorless crystals very similar in their general physical properties. Gallic acid gave the compound (V), and the potassium salt and the methyl ester were also obtained; the methyl ester was prepared by the action of methyl gallate on antimony trioxide in tartaric acid solution.



(V)

Christiansen[142] has widely extended the preparation of compounds of this class by using the antimony in the form of sodium antimonyl tartrate, which is more convenient than the potassium salt because of its greater solubility. A number of derivatives similar to (I) and (III) were obtained by boiling the appropriate 1,2-dihydric phenol with the sodium antimonyl tartrate in aqueous solution. For this purpose he employed pyrogallol, gallic acid, its amide, and various esters, 3,4,5-trihydroxybenzoylglycollic acid and its amide, 2,3-dihydroxy-5-carboxyphenoxyacetic acid, and 2,3,4-trihydroxybenzaldehyde and its phenylhydrazone. The compounds were insoluble in water and the usual solvents, and could not be purified by recrystallization; their composition depended to some extent on the conditions of their preparation, but analysis indicated that compounds approximated (usually closely) in composition to derivatives of type (I) and (III).

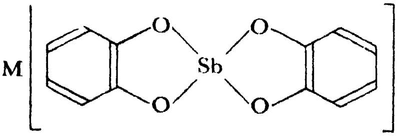
Feigl[143] has employed the pyrogallol derivative (III) for the microdetection of antimony, and also for its estimation in the presence of lead, tin, and trivalent arsenic. He finds that if pyrogallol is added to a solu-

[142] Christiansen, *J. Am. Chem. Soc.*, **48**, 1365 (1926).
[143] Feigl, *Z. anorg. Chem.*, **64**, 41 (1924).

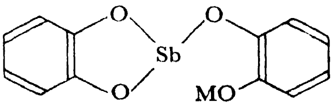
tion containing trivalent antimony which is faintly acidic with a mineral acid, the compound (III) separates as a white silky precipitate. This precipitation is incomplete in neutral, alkaline, or in acetic acid solution, but will indicate the presence of 0.025 mg. of antimony in 5 cc. of solution. To estimate antimony in the presence of the above three metals, the solution made faintly acid with hydrochloric acid is first treated with sodium potassium tartrate, and then with five times the quantity of pyrogallol theoretically required. The precipitated compound (III) is collected in a Gooch crucible, washed with water, dried at 100°, and weighed as such.

Class II

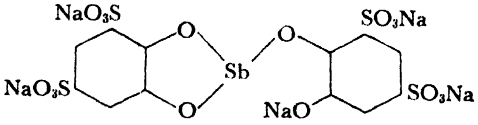
Rosenheim and Baruttschisky[144] have stated that when an alkaline solution of pyrocatechol is treated with antimony trioxide, very stable salts of type (VI) are obtained, where M indicates a monovalent metallic ion. Actually, however, analyses are given only for the crystalline water-soluble monoammonium salt. No evidence is produced to show that the ammonium salt has the constitution (VI) and not the constitution (VII) (where M represents the NH_4 ion). In this case, however, the compound may well have the constitution (VI), since an ammonium salt of a



(VI)



(VII)



(VIII)

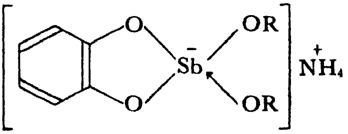
---

[144] Rosenheim and Baruttschisky, *Ber.*, **58**, 891 (1925).

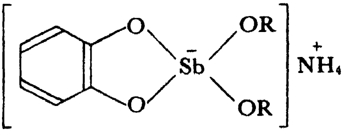
phenol—such as (VII)—would almost certainly not be sufficiently stable to separate in well-defined crystals.

A derivative of this type has been prepared from the sodium salt of pyrocatechol-3,5-disulfonic acid and has been employed as a drug under the name of Fuadin.[145] It is usually depicted as having the structure (VIII) akin to (VII), but it may have the spirocyclic structure similar to (VI). It has been employed for the treatment of schistosomiasis and filariasis; for a general account of its therapeutic application, see Schubert[136] and Bang and Hairston.[137]

A class of pyrocatechol-antimony compounds which may have a structure akin to that of compounds of type (VI) has recently been described by Wheeler and Banks.[145a] These authors have attempted to obtain soluble derivatives of *o*-phenylene hydrogen stibinate (I) for therapeutic purposes, and find that this compound in the presence of an alcohol (ROH) and ammonia or an amine gives water-soluble derivatives which they formulate as (IX), since these derivatives in aqueous solution act as salts. The formulation (IX) is, however, unlikely, as the antimony atom would now have an outer shell of eleven electrons, and it is more probable that they have the structure (X) and are thus analogous in structure to compounds of type (VI). This possibility is implied by Wheeler and Banks, for they suggest that the tartaric acid derivative of the stibinate (I) should be formulated as (XI), although no evidence in support of this structure is adduced. These alcohol compounds of type (X) when prepared from ammonia or volatile amines decompose slowly



(IX)



(X)

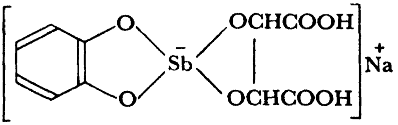
---

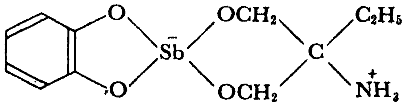
[145] Schmidt, *Med. u. Chem. Abhandl. med.-chem. Forschungsstätten I. G. Farbenind.*, **2**, 93 (1934).

[145a] Wheeler and Banks, *J. Am. Chem. Soc.*, **70**, 1264 (1948).

on standing, but when prepared from amines of lower volatility are stated to be stable to heat and storage.

Wheeler and Banks[145b] have also briefly described a similar class of compound obtained by the interaction of the stibinate (I) and various amino alcohols. If the coordinate link which these authors employ is again replaced by a covalent bond, a typical member of these series is formulated as (XII). It is stated that if equimolecular quantities of the stibinate (I) and the amino alcohol are used in the preparation, the resulting product of type (XII) is stable in the solid state, but in aqueous solution undergoes slow hydrolysis.


(XI)


(XII)

Class III

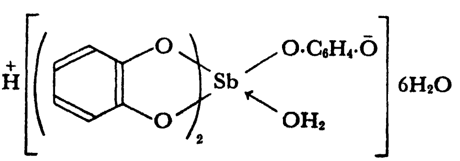
The history of compounds in this class runs closely parallel to that of the analogous arsenic compounds (p. 67). Weinland and Scholder[146] stated that antimony pentoxide and pyrocatechol reacted to form "tri-pyrocatechylantimonic acid," which formed yellowish-green crystals easily

$H_3[O{=}Sb{-}(O{\cdot}C_6H_4{\cdot}O{-})_3]6H_2O$

(XIII)

$KH_2[O{=}Sb{-}(O{\cdot}C_6H_4{\cdot}\bar{O}{-})_3]\tfrac{1}{2}H_2O$

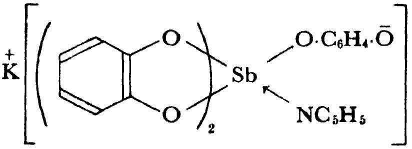
(XIV)


(XV)

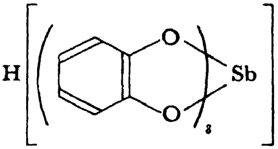
[145b] Wheeler and Banks, *J. Am. Chem. Soc.*, **70**, 1266 (1948).
[146] Weinland and Scholder, *Z. anorg. Chem.*, **127**, 343 (1923).

soluble in water. To this acid they attributed the structure (XIII), precisely similar to that which Weinland and Heinzler[147] had given to the corresponding arsenic acid. They prepared a number of salts, such as the potassium salt (XIV), and showed that the acid and its alkali salts even in hot aqueous solution were decomposed only very slowly by hydrogen sulfide.

Reihlen, Sapper, and Kall[148] pointed out that all the salts prepared by Weinland and Scholder, with the exception of some complex mercury derivatives, were salts such as (XIV) in which the acid was acting as if it were monobasic and not tribasic. Consequently, they suggested the structure (XV) for the acid, and in support of this formula they showed that—as in the case of the arsenic analog—the coordinated water molecule could be replaced by a coordinated pyridine molecule, and stable sodium and potassium pyridinotripyrocatechyl antimonates (XVI) thus obtained.



(XVI)



(XVII)

It will be recalled that in the case of tripyrocatechylarsenic acid (p. 68) to which structures analogous to (XIII) and (XV) had been attributed, Rosenheim and Plato[149] went one step further and asserted that all three pyrocatechyl units were chelated (*i.e.*, joined by two bonds) to the arsenic atom, and their optical resolution of salts of this acid provided considerable, although not decisive, evidence for this structure; the position and linkage of the one tenaciously held molecule of water remained uncertain. By analogy, one might suspect that the antimonic acid might have the analogous structure (XVII); Rosenheim and Plato were aware of this possibility but state that so far the resolution of the antimonic acid has not been achieved. Consequently, there is no concrete evidence to support structure (XVII).

[147] Weinland and Heinzler, *Ber.*, **52,** 1316 (1919).

[148] Reihlen, Sapper, and Kall, *Z. anorg. Chem.*, **144,** 218 (1925).

[149] Rosenheim and Plato, *Ber.*, **58,** 2000 (1925).

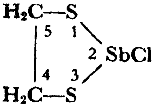
Five-Membered Ring Systems Containing Carbon, Antimony, and Sulfur

2-Stibina-1,3-dithiacyclopentanes

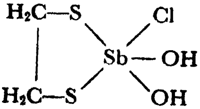
Clark[150] has shown that when 1,2-dimercaptoethane or ethanedithiol, $HS \cdot CH_2 \cdot CH_2 \cdot SH$, is added to antimony trichloride dissolved in a minimum quantity of cold concentrated hydrochloric acid, and the mixture then heated on the water bath for 15–20 minutes, 2-chlorostibina-1,3-dithiacyclopentane (I), R.I. 85, is formed; this compound separates from benzene as colorless crystals, m.p. 124°. Clark termed this compound 1-chlorocyclo-2,5-dithia-3,4-dimethylenestibine, but the name and numbering of this ring system have now been changed to bring them in line with those of the corresponding arsenic derivatives (p. 70). However, Clark's system of numbering has much to recommend it.

The addition of hydrogen peroxide to a boiling ethanolic solution of Clark's compound gives an amorphous precipitate,the composition of which indicates it to be the 2-chlorostibine dihydroxide (II).

When a mixture of equimolecular quantities of the 2-chlorostibine (I) and thioglycollic acid, $HS \cdot CH_2 \cdot COOH$, was heated in pyridine solution, the pyridine salt of 2-(carboxymethylthiostibina)-1,3-dithiacyclopentane, $(\cdot CH_2 \cdot S)_2 : Sb \cdot S \cdot CH_2COOH, C_5H_5N$, was obtained as colorless crystals, m.p. 101°, but the free acid could not be isolated in the pure state.



(I)



(II)

When the disodium salt of *m*-thiolbenzoic acid was boiled with the chlorostibine (I) in ethanolic solution, and the mixture then acidified with hydrochloric acid and cooled, colorless crystals of 2-(*m*-carboxyphenyl thiostibina)-1,3-dithiacyclopentane, $(\cdot CH_2 \cdot S)_2 : Sb \cdot S \cdot C_6H_4 \cdot COOH$, were obtained, but great difficulty was experienced in repeating the preparation of this crystalline derivative.

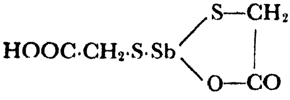
---

[150] Clark, *J. Chem. Soc.*, **1932**, 1826.

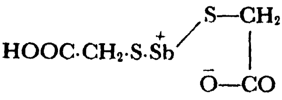
Five-Membered Ring Systems Containing Carbon, Antimony, Oxygen and Sulfur

Antimony Derivatives of Thioglycollic Acid

Klason and Carlson[151] have shown that when three equivalents of thioglycollic acid, $HS{\cdot}CH_2{\cdot}COOH$, are added to a solution of antimony trichloride in dilute hydrochloride acid, antimony thioglycollate (I), R.I. 81, separates in white monoclinic crystals, which are only moderately soluble in cold water. Ramberg[152] prepared this compound by boiling a $\frac{2}{3}N$ aqueous solution of thioglycollic acid with antimony trioxide, and also



(I)



(II)

prepared a number of salts in the formation of all of which the compound (I) was acting as a monobasic acid. Holmberg[153] confirmed the production of Klason and Carlson's compound, and refuted the earlier claim of Rosenheim and Davidsohn[154] that antimony formed a thioglycollic acid derivative of composition $Sb(S{\cdot}CH_2COOH)_3{\cdot}12H_2O$. This error was subsequently admitted by Rosenheim.[155] It is noteworthy, however, that arsenic does form a compound $As(S{\cdot}CH_2COOH)_3$, which has been described by Rosenheim and Davidsohn and also by Klason and Carlson.

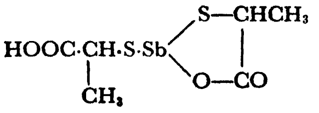
There is little doubt that the acid does contain the heterocyclic ring depicted in (I) and is not a zwitterion of type (II). This is indicated by the fact that, as stated above, it acts as a monobasic acid, and as such gives a number of salts. It also has a sharp melting point 201–202°,[156] which indicates a covalent structure such as (I) rather than an ionic structure such as (II). However, Klason and Carlson state that the antimony is held only feebly in the cyclic combination, and that, for example, the addition of ethanolic potassium hydroxide to an aqueous solution will precipitate all the antimony as potassium antimonite.

---

[151] Klason and Carlson, *Ber.*, **39**, 732 (1906).
[152] Ramberg, *Ber.*, **39**, 1356 (1906).
[153] Holmberg, *Z. anorg. Chem.*, **56**, 385 (1908).
[154] Rosenheim and Davidsohn, *Z. anorg. Chem.*, **41**, 231 (1904).
[155] Rosenheim, *Z. anorg. Chem.*, **57**, 359 (1908).
[156] Volmar and Weil, *Comp. rend.*, **207**, 534 (1938).

Formation of cyclic compounds of this type is shown by other α-mercaptocarboxylic acids. Thus, thiol-lactic acid gives a similar compound (III), m.p. 192°.[156]

As would be expected, these cyclic compounds are formed only by the free mercapto acids. If the latter are esterified, normal noncyclic derivatives of antimony are obtained. For example, the ethyl ester of thioglycollic acid, $HS{\cdot}CH_2{\cdot}COOC_2H_5$, reacts with antimony trioxide in the absence of water to give the antimony triethylthioglycollate (IV).[157,158]



(III)

$Sb(SCH_2COOC_2H_5)_3$

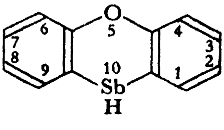
(IV)

The sodium salt of the acid (I), which is readily soluble in water, has been used as a drug to combat kala azar, schistosomiasis, and filariasis.

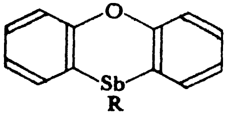
Six-Membered Ring Systems Containing Carbon, Antimony, and Oxygen

Phenoxstibines

The parent compound in this series, phenoxstibine (I), is unknown, and all derivatives which have been prepared are 10-substituted compounds of type (II): in this respect the phenoxstibines resemble the phenoxarsines (p. 100).



(I)



(II)

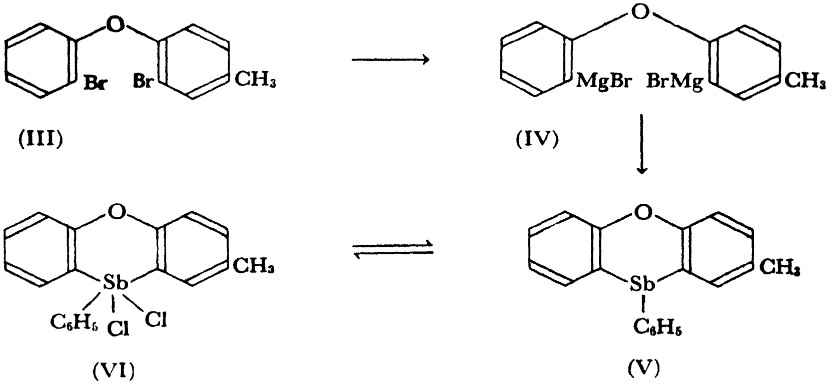
---

[157] Rowntree and Abel, *J. Pharmacol. and Exp. Therap.*, **2**, 109 (1910).

[158] Bounner, *Arch. Exp. Path. Pharmakol.*, **68**, 193 (1912).

The synthesis of the phenoxstibine ring system has been investigated by Campbell,[159] who found that methods based on those successfully used for the analogous arsenic derivatives failed in the antimony series. For example, diazotization of 2-amino-4′-methyldiphenyl ether followed by the usual Bart reaction gave only a 5–7% yield of the 4′-methyldiphenylether-2-stibonic acid, although by a similar reaction Lesslie and Turner[160] had obtained a high yield of the corresponding 2-arsonic acid (p. 104). Furthermore, attempts made to increase this yield by the modifications employed by Morgan and Davies[126,131] (p. 131, 136) gave no improvement.

The following synthesis was ultimately successful. 2,2′-Dibromo-4-methyldiphenyl ether (III) was converted into the double Grignard reagent (IV) in about 80% yield, and this reagent was then treated with



(III) (IV) (VI) (V)

phenyldi-iodostibine, $C_6H_5SbI_2$, with the formation of 2-methyl-10-phenylphenoxstibine (V). This compound was initially obtained as a crude viscous oil, b.p. 200–210°/0.5 mm., which did not crystallize. It was therefore converted to the phenoxstibine dichloride (VI), which when recrystallized from petroleum formed colorless crystals, m.p. 140–142°. This was converted back to the phenoxstibine (V) by dissolving it in ethanol and adding aqueous ammonia to the solution until a precipitate of the oxide began to appear; hydrogen sulfide was then passed through the mixture to reduce the oxide, and the 2-methyl-10-phenylphenoxstibine (V) ultimately obtained as colorless crystals, m.p. 62–63°. The over-all yield of the pure phenoxstibine (V), based on the phenyldi-iodostibine used, was 30–35%.

---

[159] Campbell, *J. Chem. Soc.*, **1947**, 4.
[160] Lesslie and Turner, *J. Chem. Soc.*, **1934**, 1170.

The prime object of the above synthesis was an investigation of the stereochemistry of the phenoxstibine ring system. Campbell points out that physical measurements show that the molecules of the antimony trihalides are pyramidal, with an intervalency angle of about 100°. This value is very close to that of arsenic, which is about 97° (p. 108). Consequently, if this intervalency angle persisted in the phenoxstibine series, it follows that the molecule (V), for example, would be folded about the O—Sb axis in precisely the manner as Lesslie and Turner's phenoxarsine compounds[160–162] were folded about the O—As axis (p. 110), and Chatt and Mann's arsanthrene compounds[163] were folded about the As—As axis (p. 122). Consequently, a phenoxstibine of type (V) should be resolvable into optically active forms if it possessed an acidic or basic group for salt formation with a suitable optically active base or acid.

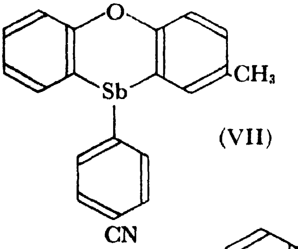
Attempts made for this purpose to oxidize the 2-methyl group in the phenoxstibine (V) to a carboxylic group proved impracticable. The di-Grignard reagent (IV) was therefore treated with *p*-cyanophenyldi-iodostibine to give 10-*p*-cyanophenyl-2-methylphenoxstibine (VII), m.p. 82°, but attempted hydrolysis of the cyano group caused disruption of the heterocyclic ring system. The use of *p*-bromophenyldi-iodostibine gave 10-*p*-bromophenyl-2-methylphenoxstibine (VIII), but the bromophenyl group in this compound would not form a Grignard reagent whereby the bromine might ultimately have been replaced by a carboxylic group. Finally, the di-Grignard reagent (IV) was treated with *p*-carbethoxyphenyldichlorostibine, $C_2H_5OOC \cdot C_6H_4 \cdot SbCl_2$, and 10-*p*-carbethoxyphenyl-2-methylphenoxstibine obtained, although never in yields greater than 10%. This ester, when hydrolyzed with ethanolic sodium hydroxide, ultimately furnished the 10-*p*-carboxyphenyl-2-methylphenoxstibine (IX). The heterocyclic ring in all these compounds proved very stable toward alkalis, but was very sensitive to acids, and even sulfur dioxide in the presence of hydrochloric acid could cause fission of the ring

---

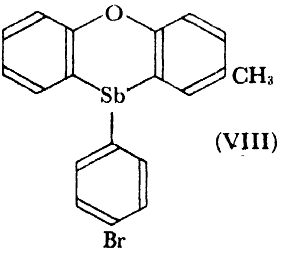
[161] Lesslie and Turner, *J. Chem. Soc.*, **1935**, 1268.
[162] Lesslie and Turner, *J. Chem. Soc.*, **1936**, 730.
[163] Chatt and Mann, *J. Chem. Soc.*, **1940**, 1184.

and even elimination of elementary antimony unless the conditions were carefully controlled.

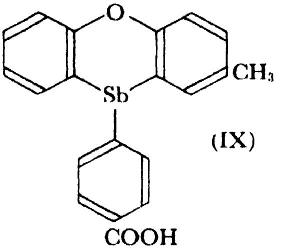
The acid (IX) was resolved into its optically active forms by means of strychnine, which gave diastereoisomeric salts of widely different solubilities. The *d*-acid was thus isolated having $[\alpha]_D + 77.5°$ in chloroform, $+ 89.6°$ in benzene, and $+ 87.6°$ in ethanol; the *l*-acid had $[\alpha]_D - 77.2°$ in chloroform and $- 89.9°$ in benzene. This acid did not possess the considerable optical stability of the phenoxarsine derivatives (p. 113).



(VII)



(VIII)



(IX)

Thus, although the acid was optically unaffected in boiling chloroform and benzene, it underwent slow racemization in boiling ethanol. Furthermore, one hour's boiling of the *dextro* acid in aqueous sodium hydroxide solution reduced the activity to $[\alpha]_D + 55.3°$, while after the ammonium salt of the *dextro* acid had been kept in aqueous solution at room temperature for 14 days it furnished the free acid having only $[\alpha]_D + 12.5°$.

The acid (IX) constitutes, therefore, the only known compound the optical activity of which is due to the disposition of the valencies of an antimony atom.

Since the compounds isolated by Campbell represent all the phenoxstibine derivatives which have yet been synthesized, their physical properties are collected in the following Table VII.

TABLE VII. Derivatives of 10-Substituted 2-Methylphenoxstibines

10-Substituent	Stibine, m.p., ° C.	Stibine dichloride, m.p., ° C.
Phenyl	62–63	140–142
p-Cyanophenyl	82	180–181
p-Bromophenyl	116	202
p-Carbethoxyphenyl	136–137	—
p-Carboxyphenyl (*dl*)	201	—
p-Carboxyphenyl (*d* and *l*)	192	—

It should be added that the *dl* acid (IX) has been tested for trypanocidal activity by administration by intravenous injection in mice infected with *Trypanosoma equiperdum*. These tests showed that the acid possessed low toxicity, but also very little trypanocidal activity.

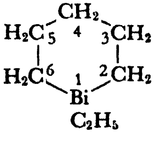
CHAPTER IV

Heterocyclic Derivatives of Bismuth

Six-Membered Ring Systems Containing Only Carbon and Bismuth

Cyclopentamethylenebismuthine

1-Ethylcyclopentamethylenebismuthine (I), R.I. 197, has been prepared by Grüttner and Wiernik[164] by a method precisely parallel to that which they employed for the preparation of the analogous phosphorus, arsenic, and antimony ring systems, *i.e.*, by the interaction of ethyldibromobismuthine, $C_2H_5BiBr_2$, and the di-Grignard reagent obtained from 1,5-dibromopentane, $CH_2(CH_2CH_2MgBr)_2$, in ethereal solution under an atmosphere of hydrogen. The tertiary bismuthine (I) was isolated as a faintly yellow-colored oily liquid, b.p. 108–112°/18–20 mm., having a very unpleasant odor. The bismuthine is very susceptible to oxidation and hence rapidly becomes cloudy on exposure to air. Grüttner and Wiernik record that a piece of paper that has absorbed the bismuthine will on exposure to the air burst into flame within a few seconds with the production of thick yellowish smoke.



(I)

---

[164] Grüttner and Wiernik, *Ber.*, **48,** 1484 (1915).

Five-Membered Ring Systems Containing Carbon, Bismuth, and Oxygen

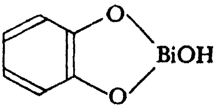
Derivatives of Pyrocatechol and Other 1,2-Dihydric Phenols

Bismuth resembles antimony in that its salts combine with the 1,2-dihydric phenols to give derivatives which almost certainly have a cyclic system containing the bismuth atom. These compounds can conveniently be divided into two classes (*cf.*, the corresponding antimony derivatives, p. 143), depending on whether the bismuth is linked to one or two dihydric phenolic residues.

The compounds in Class I are almost invariably insoluble in water and cannot be recrystallized; consequently, many remain ill-defined, and there is little precise evidence regarding their structure and complexity. The compounds in Class II, although at present few in number, are well-defined crystalline compounds whose composition is not in doubt. Their structure is discussed briefly below.

Class I

Richard[165] recognized that many 1,2-dihydric phenols would combine with bismuth salts under suitable conditions to give derivatives of type (I), which separated as insoluble citron-yellow powders. He obtained such derivatives from homocatechol, protocatechuic acid, gallic acid, and methyl gallate. He found that 1,3- and 1,4-dihydric phenols would not give compounds of this type, a fact which confirms structure (I).



(I)

Thibault also investigated the products from gallic acid,[166–168] pyrogallol-carboxylic acid,[169] and from protocatechuic acid.[170] The last acid gave a derivative as citron-yellow crystals, the composition of which was identical with that of Richard's compound.

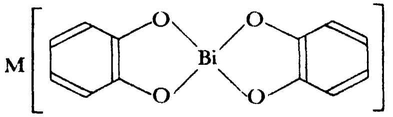
---

[165] Richard, *J. pharm. chim.* [VI], **12,** 145 (1900).
[166] Thibault, *J. pharm. chim.* [VI], **14,** 487 (1901).
[167] Thibault, *Ann. chim. et phys.* [VII], **25,** 268 (1902).
[168] Thibault, *Bull. Soc. Chim. France* [III], **29,** 531 (1903).

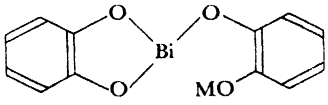
Feigl and Ordelt[171] have more recently used complex derivatives of pyrogallol to estimate bismuth, the method having the advantage that it can be employed accurately in the presence of lead. For this purpose, a solution of the salt, for example, bismuth nitrate, is treated with ammonia until it is faintly turbid, and is then boiled and treated with a slight excess of pyrogallol. The heavy yellow crystalline precipitate is collected in a Gooch crucible, washed with very dilute nitric acid and water, dried at 110°, and weighed. However, since these authors attribute the composition $C_6H_3O_3Bi$ to this precipitate, it is evidently far more complex than compounds of type (I).

Class II

Rosenheim and Baruttschisky[172] have shown that if an aqueous alkaline solution of pyrocatechol is boiled in the absence of oxygen and then saturated with bismuth hydroxide or carbonate, the solution when filtered



(II)



(III)

and cooled deposits yellow crystalline salts of composition (II) (where M represents a monovalent cation), similar to the ammonium salt which these authors isolated in the analogous antimony series (p. 146). In the bismuth series, the ammonium and sodium salts were isolated as yellow needles, and treatment of the sodium salt with barium chloride gave the corresponding barium salt as a yellow crystalline powder. In this bismuth series—as in the analogous antimony derivatives—there appears to be little doubt that the compounds do possess the spirocyclic structure (II) and not the 3-covalent bismuth structure (III) because Rosenheim and Baruttschisky were able to isolate the pyridinium salt, $C_5H_5N,H[Bi(O_2C_6H_4)_2]$, as fine clear yellow needles which were solvent-free. Clearly it is very unlikely that this salt would be of type (III), since this would involve stable salt formation between the pyridine and the phenolic groups.

---

[169] Thibault, *Bull. Soc. Chim.* [III], **29,** 680 (1903).
[170] Thibault, *Bull. Soc. Chim.* [III], **31,** 176 (1904).
[171] Feigl and Ordelt, *Z. anal. Chem.*, **65,** 448 (1925).
[172] Rosenheim and Baruttschisky, *Ber.*, **58,** 891 (1925).

It is noteworthy that the ammonium and potassium salts in this series crystallized initially with a third pyrocatechol residue. However, this could be readily removed and there is apparently no evidence that bismuth can give stable combination with three pyrocatechol units. In this respect it differs of course from arsenic and antimony (*cf.* p. 67, 148).

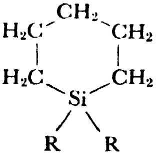
CHAPTER V

Heterocyclic Derivatives of Silicon

Six-Membered Ring Systems Containing Only Carbon and Silicon

Cyclopentamethylenesilicon Derivatives

Bygdén[173] has shown that if silicon tetrachloride is added to a chilled ethereal solution of the di-Grignard reagent prepared from 1,5-dibromopentane, *i.e.*, $CH_2(CH_2CH_2MgBr)_2$, a ready reaction occurs with the formation of cyclopentamethylenesilicon dichloride (I, R = Cl), R.I. 212. This reaction is of course very similar to that by which cyclopentamethylenephosphines, arsines, stibines, and bismuthines have been prepared. The dichloride forms a clear, pungent-smelling liquid, b.p. 168.5–170.5°/-764 mm., and burns with a greenish flame forming silicon dioxide.



(I)

When treated with water it forms a viscous mass which dries to a yellowish-brown solid: this is apparently the polymerized silicone $[(CH_2)_5\colon SiO]_n$.

When the dichloride is treated with methyl magnesium bromide, it forms dimethylcyclopentamethylene silicon (I, R = CH_3), a colorless, readily inflammable liquid, b.p. 133–134°/752.9 mm., having a faint camphorlike odor.

---

[173] Bygdén, *Ber.*, **48**, 1236 (1915).

Bygdén treated the above di-Grignard reagent, $CH_2(CH_2CH_2MgBr)_2$, with diethyldichlorosilicon, $(C_2H_5)_2SiCl_2$, but obtained only a small yield of impure diethylcyclopentamethylenesilicon (I, R = C_2H_5), b.p. 184–194°. Grüttner and Wiernik[174] state that this compound is better prepared, although only in moderate yield, by the condensation of 1,5-dibromopentane and diethyldichlorosilicon with sodium in ether, but no experimental details are given.

---

[174] Grüttner and Wiernik, *Ber.*, **48**, 1474 (1915).

INDEX

A

2-(*p*-Acetamidophenylarsa)-1,3-dithiacyclopentane, 71
p-Acetamidophenyl arsenoxide, 71
Acetone, condensation with phosphorus trichloride, 13
10-Acetoxy-5,10-dihydrophenarsazine, 82
5-Acetyl-10-chloro-5,10-dihydrophenarsazine, 84
Acridarsine, 50
Acridarsinic acid, 50
Adamsite, 98. *See also* 10-Chloro-5,10-dihydrophenarsazine.
Alkyl arsonic acids, 5, 62
  condensation with
    o-dihydroxybenzenes, 62
    glycols, 62
    α-hydroxycarboxylic acids, 62
5-Aminoacenaphthene, 94
2-Aminoarsanthrenic acid, 120
2-Aminobiphenyl, 37, 131
2-Amino-5,10-dichloro-5,10-dihydroarsanthrene, 120
  hydrochloride, 120
o-Aminodiphenylarsinic acid, 125
2-Aminodiphenyl ether, 102
2-Aminodiphenylmethane, 50, 136
2-Aminodiphenyl sulfide, 115
3-Amino-4-hydroxyphenylarsenoxide hydrochloride, 72
2-Amino-4′-methyldiphenyl ether, 153
8-Amino-5-nitroquinoline, 94
  condensation with *o*-bromophenylarsonic acid, 94
Aminophenazarsinic acids, 84
o-Aminophenylarsonic acid, 90, 118
o-Aminophenyl-*p*-tolyl ether, 108
Anhydride of
  bis(2-biphenylyl)hydroxystibine, 133
  bis(2-diphenylmethane)hydroxystibine, 138
  5,10-dihydroxy-5,10-dihydroarsanthrene, 75, 119
  10-hydroxy-5,10-dihydrophenarsazine, 81, 88
Anhydride of (*continued*):
  10-hydroxy-5,10-dihydrostibacridine, 137
  10-hydroxyphenoxarsine, 101
  9-hydroxystibinafluorene, 132
  o-phenylene-bis(arsonous chloride), 75
Anhydrides of *o*-carboxyphenyl arsinous and arsinic acids, 58
Anilinodichlorophosphine oxide, 15, 16
Anilinoethylenediaminophosphine oxide, 15
Anilino-*o*-phenylenediaminophosphine oxide, 15
2-*p*-Anisylisoarsindoline, 34
  hydroxy nitrate, 34
  hydroxy picrate, 34
  methiodide, 34
  methopicrate, 34
  oxide, 34
p-Anisylphenyl-2-(*o*-methoxymethylphenyl)ethylphosphine, 12
p-Anisyl-phenyl-monochlorophosphine, 12
Anthranilic acid, 89
Anti-Lewisite, British. *See* BAL.
Antimony
  derivatives of
    1,2-dihydric phenols, 143
    pyrocatechol, 143
  heterocyclic derivatives, 129
  microdetection and estimation, 145
  thioglycollic acid derivatives, 151
Antimonyl tartrates, 140
  structure, 140–143
  therapeutic action, 143
Antimony thioglycollate, 151
  sodium salt, therapeutic action, 152
Antimony tribromide, reaction with pyrocatechol, 144
Antimony trichloride
  reaction with
    ethanedithiol, 150
    pyrocatechol, 143, 144
    pyrogallol, 144
Antimony triethylthioglycollate, 152

Antimony trioxide, 146, 151
  reaction with
    pyrocatechol, 146
    thioglycollic acid, 151
Arsa, use in nomenclature, 3
10-Arsa-anthracene, 3
Arsa-carbazole, 37
6-Arsa-1,2,3,4-dibenzcyclohepta-1,3-dienes, 57
  absorption spectra, 56
  preparation, 58
Arsacridines, 3, 49
Arsacridinic acid, 3, 50
  reduction, 50
Arsacridones, 51
2-Arsa-1,3-dithiacyclopentanes, 70
  nomenclature, 70
  preparation, 71
  therapeutic action, 72, 73
Arsafluorenes, 25, 36, 37
  nomenclature, 36, 37
  numbering, 36
9-Arsafluorene, 36, 37
  nomenclature, 36, 37
Arsafluorinic acid, 37
  reduction, 37
Arsanthrene, 117, 119. *See also* 5-Substituted 5,10-dihydroarsanthrenes.
  numbering, 118
Arsanthrene derivatives, 118
  stereochemistry, 121
Arsanthrene oxide, 76, 119, 126
  reduction, 119
Arsanthrenic acid, 118, 120
Arsanthridines, 52
  numbering, 52
  preparation, properties, and structure, 52, 53
2-Arsaperinaphthanes, 55
  absorption spectra, 56
  preparation, 55
  stability, 57
2-Arsaperinaphthindanes, 55. *See* 2-Arsaperinaphthanes.
4-Arsa-1,2,3,4-tetrahydroarsinoline, 116
Arsedine, 38
Arsenic, heterocyclic derivatives, 25
Arsenic acid
  condensation with
    ethylene glycol, 64, 65
    pinacol, 65
    pyrocatechol, 67
Arsenic atom, intervalency angle, 108
Arsenic trichloride
  reaction with
    2-bromostyrene, 28
    o-dibromobenzene, 119
    di-(1-naphthyl)amine, 88
    di-(2-naphthyl)amine, 88
    diphenylamine, 80, 105
    diphenyl ether, 101, 105
    diphenylmethylamine, 86, 90
    dithiols, 74
    ethane-1,2-dithiol, 74
    methyl iodide and aqueous sodium hydroxide, 5
    2-naphthylamine, 88
    phenylacetylene, 29
    1-phenyl-2-(diethylaminomethyl)-acetylene, 27
    phenyl-1-naphthylamine, 86
    phenyl-1-naphthyl ether, 107
Arsenoles, 25
Arsenolidine, 25
γ-*p*-Arsenophenylbutyric acid, 73
  condensation with BAL, 73
Arsenosobenzene. *See* Phenylarsenoxide
Arsepidine, 38
Arsindoles, 25, 26
Arsindolines, 30
  preparation and properties, 30, 31
  therapeutic action, 33, 34
Arsines, tertiary,
    palladium derivatives 77
    preparation, 5
    tin derivatives, 80
Arsine dichlorides, tertiary, 66
    structure, 66
Arsine dihydroxides, tertiary, 66
Arsine oxides, tertiary, 5
    reduction, 5
Arsinic acids, 2
  nomenclature, 2
  preparation by Meyer reaction, 5
Arsinoacetic acid and methyl ester, 64, 65
  condensation with
    pyrocatechol, 64
    ethylene glycol, 65
    pinacol, 66
    d-tartaric acid, 66
Arsinous acids, 2
  nomenclature, 2

Arsonic acids, 2
  nomenclature, 2
  preparation by Bart and Meyer reactions, 5, 6
2-Arsono-3′-aminodiphenylarsinic acid, 120
o-Arsonodiphenylarsinic acid, 118
2-Arsono-3′-nitrodiphenylarsinic acid, 120
Arsonium salts, dissociation equilibrium, 47
Arsonous acids, 2
  nomenclature, 5
Aryl arsonic acids, 6
  condensation with
    o-dihydroxybenzenes, 62
    glycols, 62
    1-hydroxycarboxylic acids, 62
5-Aza-10-arsa-anthracene, 80
1-Aza-10-chloro-5,10-dihydrophenarsazine, 99
Azaphenarsazines, 99
Azarsinic acids, 100
Azarsinyl chlorides, 100

B

BAL (British Anti-Lewisite), 71. *See also* 2,3-Dithiopropanol.
  biochemical action, 72, 73
  chemistry, 72
  pharmacology, 72, 73
  toxicology, 72
Barium antimonyl tartrate, 141
Bart reaction, 5
Bart-Schmidt reaction. *See* Bart reaction.
Benzarsenious oxide hydrate, 59
2,3-Benzarsindoles, 36, 37
3,4-Benz-10-*d*-bromocamphorsulfonate-5,10-dihydrophenarsazine, 97
3,4-Benz-10-bromo-5,10-dihydrophenarsazine, 86
1,2-Benz-10-chloro-5, 0-dihydrophenarsazine, 98
3,4-Benz-10-chloro-5,10-dihydrophenarsazine, 86, 92, 97
  stereochemistry, 97
3,4-Benz-10-chlorophenoxarsine, 107
3,4-Benz-10-(2-chlorovinyl)-5,10-dihydrophenarsazine, 86, 92
3,4-Benz-10-iodo-5,10-dihydrophenarsazine, 86
5-Benzoyl-10-chloro-5,10-dihydrophenarsazine, 84
Biphenylyl-2-arsonic acid, 37
  cyclization, 37
  reduction, 37
Biphenylyl-2-diazonium antimony tetrachloride, 131
2-Biphenylyldichloroarsine, 37, 38
Biphenylyl-2-(dichlorostibine), 131, 132
  cyclization, 131
  dismutation, 132
Biphenylyl-2-(di-iodostibine), 131
2,2′-Biphenylylenearsines, 37
2-Biphenylylmethanol, 53
2-Biphenylylmethyl bromide, 53
  reaction with phenylarsinebis(magnesium bromide), 53
2-Biphenylylmethyl chloride, 54
  Grignard derivative, 54
(2-Biphenylylmethyl)phenylchloroarsine, 53
  cyclization, 53
9-(2-Biphenylyl)stibinafluorene, 134
9-(2-Biphenylyl)stibinafluorene dichloride, 134
  reduction, 134
Biphenylyl-2-stibonic acid, 131
  cyclization, 132
Bis(2-biphenylyl)hydroxystibine, 133
Bis(2-biphenylylmethyl)phenylarsine, 53
  dichloride, thermal decomposition, 53
Bis(2-biphenylyl)monochlorostibine, 133
Bis(2-biphenylyl)monoiodostibine, 133
Bis(2-biphenylyl)trichlorostibine, 134
  cyclization, 134
1,8-Bis(bromomethyl)naphthalene, 55
2,2′-Bis(10-chloro-5,10-dihydrophenarsazine), 94
As-spiro-Bis-5-chloroisoarsindolinium bromide, 35, 36
  attempted optical resolution, 36
Bis(2-diphenylmethane)hydroxystibine, 138
  anhydride, 138
Bis(2-diphenylmethane)monochlorostibine, 138
Bis(2-diphenylmethane)trichlorostibine. 138
  cyclization, 139

10,10′-Bis-5,10-dihydrophenarsazine, 85
  suggested dissociation, 85
Bis-1,2-hydrazino-bis(anilinophosphine oxide), 16
As-spiro-Bis-isoarsindolinium bromide, 35
  iodide, 35
  picrate, 35
Bis-2-isoarsindolyl sulfide, 35
10,10′-Bisphenoxarsine, 102
Bismuth
  derivatives of
    1,2-dihydric phenols, 158
    pyrocatechol, 158
  estimation as pyrogallol derivative, 159
  heterocyclic derivatives, 157
As-spiro-Bis-1,2,3,4-tetrahydroisoarsinolinium bromide, 36, 48
  d-bromocamphor sulfonate, 49
  iodide, 49
  optical resolution, 49
British Anti-Lewisite (BAL), 71. *See also* 2,3-Dithiolpropanol.
o-Bromobenzyl methyl ether, 11
  Grignard derivative, 11
1-Bromo-3-chloro-2(diethylaminomethyl)arsindole hydrobromide, 27
1-Bromocyclopentamethylenearsine, 40
10-Bromo-5,10-dihydrostibacridine, 138
o-(2-Bromoethyl)benzyl methyl ether,, 45
  reaction with
    methyldichloroarsine, 45
    phenyldichloroarsine, 45
2-Bromoethylphthalimide, 82
2-*o*-(Bromomethyl)benzyl-2-methylisoarsindolinium bromide, 35
  thermal dissociation, 35
10-Bromophenoxarsine, 101
2-Bromophenyl-2′-aminophenylarsinic acid, 88
  cyclization, 88, 89
o-Bromophenylarsonic acid
  condensation with
    5-aminoacenaphthene, 94
    8-amino-5-nitroquinoline, 94
    aniline, 90
    anthranilic acid, 89
    benzidine, 94
    monomethylaniline, 91
    o-, *m*-, and *p*-phenylenediamine, 94
o-Bromophenylarsenoxide, 88
p-Bromophenyl-*p*-chlorophenyl-phenyl-4-*o*-xylylarsonium *l*-tripyrocatechylarsenate, 70
o-Bromophenyldichloroarsine, 119
p-Bromophenyldi-iodostibine, 154
  reaction with 2,2′-dibromo-4-methyldiphenyl ether Grignard derivative, 154
10-*p*-Bromophenyl-2-methylphenoxstibine, 154
2-Bromophenyl-2′-nitrophenylarsinic acid, 88
p-Bromophenyl-phenyl-2-(*o*-methoxymethylphenyl)ethyl phosphine, 11
p-Bromophenyl-phenyl-monochlorophosphine, 11
2-*p*-Bromophenyl-2-phenyl-1,2,3,4-tetrahydroisophosphinolinium bromide, 12
  d-camphor sulfonate, 12
  picrate, 12
2-Bromostyrene, 28

C

p-Carbethoxyphenyldichlorostibine, 154
  reaction with 2,2′-dibromo-4-methyldiphenyl ether Grignard derivative, 154
10-*p*-Carbethoxyphenyl-2-methylphenoxstibine, 154
4-Carboxy-10-chloro-5,10-dihydrophenarsazine, 89
2-Carboxy-10,10-dimethylphenoxarsonium iodide, 111
2-Carboxydiphenylamine-2′-arsonic acid, 89
2-Carboxydiphenylaminedichloroarsine, 89
o-Carboxydiphenylarsinic acid, 29, 52
2-Carboxy-10-ethyl-10-methylphenoxarsonium iodide, 111
Carboxymethylarsonic acid and methyl ester, 64
  condensation with
    ethylene glycol, 65
    pinacol, 66
    pyrocatechol, 64
    d-tartaric acid, 66
10-Carboxymethyl-10-methylphenoxarsonium bromide, 106
2-(Carboxymethylthioarsa)-1,3-dithia-

cyclopentane, 75
2-(Carboxymethylthiostibina)-1,3-dithiacyclopentane, pyridine salt, 150
2-Carboxyphenoxarsinic acid, 108
2(*p*-Carboxyphenylarsa)-1,3-dithiacyclopentane, 71
o-Carboxyphenylarsinic acid, 58
  cyclization, 58
o-Carboxyphenylarsinous acid, 58
  cyclization, 58
o-Carboxyphenylarsonous acid, 59
  anhydride, 59
  cyclization, 59
10-*p*-Carboxyphenyl-2-chloro-phenoxarsine, 112
  optical activity, 113
  oxide, 113
  preparation, 113
o-Carboxyphenyldichloroarsine, 59
  anhydride, 59
  cyclization, 59
o-Carboxyphenylmethylarsinic acid, 60
  anhydride, 60
o-Carboxyphenylmethylchloroarsine, 59
  anhydride, 60
  cyclization, 59
10-*p*-Carboxyphenyl-2-methylphenoxstibine, 113, 154
  optical resolution and stability, 154, 155
  strychnine salt, 155
  therapeutic action, 156
o-Carboxyphenylphenylchloroarsine, 60
  anhydride, 60
2-Carboxy-10-phenylphenoxarsine oxide, 112
o-Carboxyphenylphenylarsinic acid, 60
  oxy-anhydride, 60
2-(*m*-Carboxyphenylthiostibina)-1,3-dithiacyclopentane, 150
p-3-Carboxypropylphenylarsenoxide, 73
  condensation with BAL, 73
Chloramine-T, 84
  reaction with 10-chloro-5,10-dihydrophenarsazine, 84
-Chloro-2-aminodiphenyl ether, 104
3-Chloroarsacridinic acid, 51
10-Chloroarsacridone, 52
2-Chloroarsa-1,3-dithiacyclopentane, 74
  condensation with thioglycollic acid, 75
9-Chloroarsafluorene, 37
9-Chloroarsafluorene (*continued*):
  hydrolysis, 38
  reaction with magnesium methyl iodide, 38
1-Chloroarsindole, 27
10-Chloro-2-bromophenoxarsine, 105
3-Chloro-10-cyano-5,10-dihydroarsacridine, 51
1-Chlorocyclo-2,5-dithia-3,4-dimethylenestibine, 150
  oxidation to dihydroxide, 150
  reaction with thioglycollic acid, 150
1-Chlorocyclopentamethylenearsine, 39, 40
1-Chlorocyclopentamethylenestibine, 135
1-Chlorocyclotetramethylenearsine, 26
10-Chloro-5,10-dihydroarsacridine, 50
  structure, 51
  vesicant action, 51
10-Chloro-5,10-dihydrophenarsazine, 80, 83
  acylation, 84
  crystal forms, 98
  nitration, 83
  oxidation, 84
  preparation, 81, 87, 88, 90
  properties, 88
  reaction with Grignard derivatives, 93
  reduction, 85
  structure, 85, 88
10-Chloro-5,10-dihydrophenphosphazine, 20
10-Chloro-5,10-dihydrostibacridine, 137
  dichloride, 137
10-Chloro-1,8-dimethyl-5,10-dihydrophenarsazine, 92
10-Chloro-1,3-dimethylphenoxarsine, 105
10-Chloro-1,4-dimethylphenoxarsine, 105
10-Chloro-2,4-dimethylphenoxarsine, 105
10-Chloro-2,8-dinitrophenazarsinic acid, 84
3'-Chlorodiphenylether-2-arsonic acid, 104
  cyclization, 104
4'-Chlorodiphenylether-2-arsonic acid, 103
  cyclization, 103
5-Chlorodiphenylether-2-arsonic acid, 104
2'-Chlorodiphenylether-2-(dichloroarsine), 102
3'-Chlorodiphenylether-2-(dichloroarsine), 102, 103, 121

4′-Chlorodiphenylether-2-(dichloroarsine), 102
5-Chlorodiphenylether-2-(dichloroarsine), 104
o-2-Chloroethylbenzyl methyl ether, 11
2-Chloroisoarsindoline, 34
10-Chloro-2-methoxyphenoxarsine, 105
10-Chloro-2-methyl-5,10-dihydroarsacridine, 51
10-Chloro-3-methyl-5,10-dihydroarsacridine, 51
10-Chloro-1-methyl-5,10-dihydrophenarsazine, 92
10-Chloro-5-methyl-5,10-dihydrophenarsazine, 90, 91
5-Chloro-2-methylisoarsindoline, 35
  reaction with 4-chloro-*o*-xylylene dibromide, 35
10-Chloro-2-methylphenoxarsine, 112
10-Chloro-3-methylphenoxarsine, 105
10-Chloro-4-methylphenoxarsine, 105
5-Chloro-2-nitrodiphenyl ether, 104
10-Chloro-4-nitrophenarsazine, 84
p-Chlorophenacyl bromide, 11
  combination with
    tertiary arsines, 47
    tertiary phosphines, 11
2-*p*-Chlorophenacyl-2-phenyl-1,2,3,4-tetrahydroisoarsinolinium bromide, 47
    optical resolution, 48
  d-bromocamphor sulfonate, 48
  iodide, 48
  picrate, 48
2-*p*-Chlorophenacyl-2-*p*-tolyl-1,2,3,4-tetrahydroisophosphinolinium bromide, 11
10-Chlorophenoxarsine, 100, 105
  action of Grignard reagents, 106
  preparation and properties, 101
  physiological action, 101
  structure, 102
10-Chlorophenoxarsine-2-carboxylic acid, 108
2-Chlorophenoxarsinic acid, 103
10-Chlorophenthiarsine, 114
  synthesis, 114, 115
3-Chloro-1-phenylarsindole, 29
  ethiodide, 29
  mercurichloride, 29
  methiodide, 29
  picrate, 29
2-*p*-Chlorophenylisoarsindoline, 34
  hydroxy nitrate, 34
  hydroxy picrate, 34
  methiodide, 34
  methopicrate, 34
  oxide, 34
10-Chloro-5-propionyl-5,10-dihydrophenarsazine, 84
2-Chlorostibina-1,3-dithiacyclopentane, 150
  oxidation, 150
  reaction with thioglycollic acid, 150
9-Chlorostibinafluorene, 131, 132
  hydrolysis, 132
1-Chloro-1,2,3,4-tetrahydroarsinoline, 45
2-Chloro-1,2,3,4-tetrahydroisoarsinoline, 46
1-Chlorovinylcyclopentamethylenearsine, 41
  dichloride, 41
2-Chlorovinyldichloroarsine, 27, 41, 86, 87, 92
10-(2-Chlorovinyl)-5,10-dihydrophenarsazine, 87, 92
4-Chloro-*o*-xylylene dibromide, 35
  reaction with methyldichloroarsine, 35
Coordinate link, 4
9-Cyanoarsafluorene, 38
1-Cyano-3-chloro-2-(diethylaminomethyl)arsindole, 27
10-Cyano-5,10-dihydroarsacridine, 51
10-Cyano-5,10-dihydrophenarsazine, 82
p-Cyanophenyldi-iodostibine, 154
  reaction with 2,2′-dibromo-4-methyldiphenyl ether Grignard derivative, 154
10-*p*-Cyanophenyl-2-methylphenoxstibine, 154
Cyclization of diphenylether-2-(dichloroarsines), 102–105
Cyclo-2,5-dithia-3,4-dimethylenearsines, 70
Cycloethylenethioarsinites, 70

Cyclohexanol-1-carboxylic acid, 62
  condensation with arsonic acids, 62, 63
Cyclopentamethylenearsines, 38
  preparation and properties, 39
  stability of ring system, 41, 42
Cyclopentamethylenearsinic acid, 40
Cyclopentamethylenebismuthines, 157
Cyclopentamethylenephosphines, 10
Cyclopentamethylenesilicon derivatives, 161
Cyclopentamethylene silicon dichloride, 161
  preparation and properties, 161
  reaction with
    methyl magnesium iodide, 161
    water, 161
Cyclopentamethylenestibines, 134
Cyclotetramethylenearsines, 25
Cyclotetramethylenephosphines, 9
Cyclotetramethylenestibines, 129

D

Diarsafluorene oxide, 38
5,10-Diarsa-anthracene, 119
1,2,8,9-Dibenz-10-chloro-5,10-dihydrophenarsazine, 88
3,4,6,7-Dibenz-10-chloro-5,10-dihydrophenarsazine, 88
1,2,3,4-Dibenzcyclohepta-1,3-diene, 57
o-Dibromobenzene, 119
Dibromobis(10-phenyl-9, 10-dihydroarsanthridine)palladium, 53
1,4-Dibromobutane, 129
  Grignard derivative, 129
2,2-Di(bromomethyl)-biphenyl, 58
2,2′-Dibromo-4-methyldiphenyl ether, 153
  Grignard derivative, 153
1,8-Di(bromomethyl)-naphthalene, 55
1,5-Dibromopentane
  Grignard derivative, reaction with
    diethyldichlorosilicon, 162
    ethyldibromobismuthine, 157
    methyldichloroarsine, 39
    phenyldichloroarsine, 39
    phenyldichlorophosphine, 10
    phenyldichlorostibine, 134
Di-*o*-carboxyphenylarsinic acid, 61
  anhydride, 61
Di-*o*-carbmethoxphenylchloroarsine, 61
Di-*o*-carboxyphenylchloroarsine, 61
  anhydride, 61
o-Dichloroarsinodiphenylchloroarsine, 118
  cyclization, 118
Dichlorobis(10-phenyl-9,10-dehydroarsanthridine)palladium, 53
1,3-Dichloro-2(diethylaminomethyl)-arsindole, 27
  hydrochloride, 27
2,2′-Dichlorodiethyl sulfide, 114
  reaction with phenylarsinebis(magnesium bromide), 114
3,10 - Dichloro - 5,10 - dihydroarsacridine, 51
5,10-Dichloro-5,10-dihydroarsanthrene, 76, 118, 119
  attempted nitration, 120
  hydrolysis and cyclization, 76
  oxidation, 120
  reaction with
    sodium carbonate, 119
    zinc and hydrochloric acid, 119
  stereochemistry, 121
1,5-Dichloro-*n*-hexane, 41
2,4-Dichloronitrobenzene, 103
1,5-Dichloropentane, 135
  Grignard derivative, 135
2,10-Dichlorophenoxarsine, 102, 103
3,10-Dichlorophenoxarsine, 103, 104
4,10-Dichlorophenoxarsine, 102
Dicyclopentamethylenearsine oxide, 40
Diethylcyclopentamethylenesilicon, 162
Diethyldichlorosilicon, 162
Diethylenedioxyarsenic acid, 64
  brucine salt, 64
  hydrolysis, 64
  molecular weight, 64
  pyridine salt, 64
1,2-Dihydric phenols
  derivatives with
    antimony, 143–148
    arsenic, 64, 67
    bismuth, 158, 159
    phosphorus, 17–19
5,10-Dihydroarsacridines, 50
  synthesis and properties, 50–52
5,10-Dihydroarsanthrene, 118

9,10-Dihydroarsanthridines, 52
  synthesis and structure, 53, 54
9,10-Dihydro-9-arsaphenanthrenes, 52
Dihydroarsedine, 41
Dihydroarsindoles, 30
4,5-Dihydro-1,3,2-dithiarsenoles, 70
Dihydroisoarsindoles, 30
3,4-Dihydroisoarsinoline, 46
5,10-Dihydrophenarsazines, 51
5,10-Dihydrophenphosphazines, 19
5,10-Dihydrostibacridines, 136
2,3-Dihydroxy-5-carboxyphenoxyacetic acid, 145
5,10-Dihydroxy-5,10-dihydroarsanthrene anhydride, 75, 119
1,2-Dimercaptoethane, 150. *See also* Ethanedithiol.
  reaction with antimony chloride, 150
9,9-Dimethylarsafluorenonium iodide, 38
Dimethylarsinic acid, 5
1,2-Dimethylcyclopentamethylenearsine, 41
  methiodide, 41
  methochloride, 41
  methopicrate, 41
1,1-Dimethylcyclopentamethylenearsonium iodide, 39
  picrate, 39
Dimethylcyclopentamethylenesilicon, 161
10,10-Dimethyl-9,10-dihydroarsanthridinium iodide, 54
10,10-Dimethyl-5,10-dihydrophenarsazonium iodide, 93
1,4-Dimethylethylene-*o*-phenylenediarsine dimethobromide, 116
1,4-Dimethylethylene-*o*-phenylenediarsine dimethopicrate, 117
Dimethyliodoarsine, 30, 43, 54
  reaction with
    2-biphenylylmethyl chloride Grignard derivative, 54
    2-phenylethyl bromide Grignard derivative, 30
    3-phenylpropyl bromide Grignard derivative, 43
Dimethylmonochloroarsine, 5
  use in Meyer reaction, 5
10,10-Dimethylphenoxarsonium iodide, 106
Dimethylphenylarsine, 32
Dimethyl-*o*-phenylbenzylarsine, 54
  dichloride, thermal decomposition 54
As,As-Dimethyl-*o*-phenylenetrimethylenediarsine, 127
  dimethobromide, 127
  dimethopicrate, 127
Dimethyl-2-phenylethylarsine, 30
  dichloride, 30
2,10-Dimethyl-10-phenylphenoxarsonium iodide, 111
Dimethyl(3-phenylpropyl)arsine, 43
  additive compound with dimethyliodoarsine, 43
  dichloride, 43
  methiodide, 43
Dimethylstyrylarsine, 28
  dichloride, 28
1,1-Dimethyl-1,2,3,4-tetrahydroarsinolinium iodide, 44
  dissociation in solution, 44
Di(1-naphthyl)amine, 88
  reaction with arsenic trichloride, 88
Di(2-naphthyl)amine, 88
  reaction with arsenic trichloride, 88
Diphenylamine
  condensation with
    arsenic trichloride, 80, 92
    arsenious oxide, 88
    2-chlorovinyldichloroarsine, 87, 92
    phosphorus trichloride, 20
Diphenylamine-2-arsonic acid, 90
Diphenylarsinic acid, 1
  formula, 1
Diphenyl-bis-1,2-hydrazinodiphosphinate, 16
Diphenyl-bis-1,2-hydrazinodithiophosphinate, 17
o-Diphenylenediarsinic acid, 118
Diphenyl ether, 101
  reaction with arsenic trichloride, 101
Diphenylether-2-arsonic acid, 102, 105
Diphenylether-2-(dichloroarsine), 102
  cyclization, 102
2-Diphenylether-methylchloroarsine, 106
Diphenylmethane-2-arsonic acid, 50
  cyclization, 50
Diphenylmethane-2-(dibromostibine), 137
Diphenylmethane-2-(dichlorostibine), 137, 138
  dismutation, 138
10-(2-Diphenylmethane)-5,10-dihydrostibacridine dichloride, 139
10-(2-Diphenylmethane)-5,10-dihydrostibacridine oxide, 139

Diphenylmethane-2-(di-iodostibine), 137
Diphenylmethane-2-(stibine oxide), 137
Diphenylmethane-2-stibonic acid, 137
  cyclization, 137
Diphenylmethylamine, 86
  reaction with arsenic chloride, 86
Diphenylmethylamine-2-arsonic acid, 91
Diphenylmonochloroarsine, 81
  formula, 1
Diphenylsulfide-2-arsine oxide, 116
Diphenylsulfide-2-arsonic acid, 115
Diphenylsulfide-2-(dichloroarsine), 116
  cyclization, 116
o,o'-Diphenylylenearsines, 36
Dissociation equilibrium of arsonium salts, 47
5,10-Disubstituted-5,10-dihydroarsanthrenes, 121
1,2-Ditertiary arsines, 77
  coordination with metals, 77
1,3-Dithia-2-arsacyclopentanes, 71
  preparation and properties, 71, 72
2,3-Dithiolpropanol, 71. *See also* BAL.
1,2-Dithiols, 71
  biochemical action, 72
  condensation with dichloroarsines, 71
  pharmacology, 72
  therapeutic action, 72
  toxicology, 72
1,3-Dithiols, 72
  condensation with dichloroarsines, 72
5,10-Di-*p*-tolyl-5,10-dihydroarsanthrene, 122
  dibromide, structure, 125
  monomethiodides, 123
  monosulfide, 125
  preparation and properties, 122
  stereochemistry, 122, 123
  tetrabromide, 124
  tetrahydroxide, 124

E

Ethanedithiol, 71, 150
  reaction with
    p-acetamidophenyl arsenoxide, 71
    antimony chloride, 150
    arsenic trichloride, 74
10-Ethoxy-5,10-dihydrophenphosphazine, 21
1-Ethylarsindole, 28
  picrate, 28
1-Ethylcyclopentamethylenearsine, 39, 41
  cyanogen bromide addition product, 41
  hydroxy bromide, 41
  methiodide, 41
1-Ethylcyclopentamethylenebismuthine, 157
  preparation and properties, 157
Ethyldibromobismuthine, 157
  reaction with 1,5-dibromopentane Grignard derivative, 157
10-Ethyl-5,10-dihydrophenarsazine, 93
  nitrosation, 94
Ethylene-1,2-bis(di-*n*-butylarsine), 77
Ethylene-1,2-bis(di-*n*-butylarsine)dichloropalladium, 78
Ethylene-1,2-bis(*n*-butylphenylarsine)-dichloropalladium, 78
  stereochemistry, 78
Ethylene-1,2-bis(*n*-butylphenylarsine sulfide), 78
  stereochemistry, 78
Ethylene-1,2-bis(di-*n*-butylarsine), 77, 117
Ethylene-1,2-bis(dimethylarsine), 77
Ethylene-1,2-bis(diphenylarsine), 77
Ethylene-1,2-bis(diphenylarsine)dichloropalladium, 78
Ethylenediamine, 15, 16
  reaction with phosphorus compounds, 15, 16
Ethylene dibromide, 116
  reaction with *o*-phenylenebis(dimethylarsine), 116
Ethylene glycol, 22
  condensation with
    arsenic acid, 64
    arsinoacetic acid, 65
    phosphorus trichloride, 22, 23
Ethylene oxide, 11
Ethylene-*o*-phenylenediarsine, 116
10-Ethyl-5-nitroso-5,10-dihydrophenarsazine, 94
10-Ethylphenoxarsine, 102, 106
  bromoacetic acid addition product, 107
  dihydroxide, 107
  ethiodide, 107
  methiodide, 107
  sulfide, 107
10-Ethylphenoxarsine-2-carboxylic acid, 111
  optical resolution, 111

F

Filariasis, 147, 152

Five-membered ring systems
  containing
    only carbon and antimony, 129
    only carbon and arsenic, 25
    only carbon and phosphorus, 9
    carbon, antimony, and oxygen, 140
    carbon, antimony, oxygen, and sulfur, 151
    carbon, antimony, and sulfur, 150
    carbon, arsenic, and oxygen, 58
    carbon, arsenic, and sulfur, 70
    carbon, bismuth, and oxygen, 158
    carbon, oxygen, and two arsenic atoms, 75
    carbon, palladium, and two arsenic atoms, 77
    carbon, phosphorus, and nitrogen, 14
    carbon, phosphorus, and oxygen, 17
Four-membered ring systems
  containing
    carbon, phosphorus, and oxygen, 13
Fuadin, 147

G

Gallic acid, 145, 158
  antimony derivatives, 145
  bismuth derivatives, 158

H

Homocatechol, 158
Hydrazine, 16
  reaction with phosphorus compounds, 16
1-Hydroxy-3-chloro-2(diethylaminomethyl)arsindole hydrochloride, 27
10-Hydroxy-5,10-dihydrophenarsazine, 81
10-Hydroxy-5,10-dihydrophenphosphazine, 19, 20
10-Hydroxy-5,10-dihydrostibacridine, 137
  anhydride, 137
o-2-Hydroxyethylbenzyl methyl ether, 11
10-(2-Hydroxyethylthio)-5,10-dihydrophenarsazine, 96
4-Hydroxymethyl-2(3′-amino-4′-hydroxyphenylarsa)-1,3-dithiacyclopentane hydrochloride, 72
  therapeutic action, 73
4-Hydroxymethyl-2(*p*-3-carboxypropylphenylarsa)-1,3-dithiacyclopentane, 73
4-Hydroxymethyl-2-(2′-chlorovinylarsa)-1,3-dithiacyclopentane, 72
2-Hydroxy-2-phenylisoarsindolinium nitrate, 33
o-Hydroxyphenyl-*o*-phenylene phosphite, 18
2-Hydroxy-2-phenyl-1,2,3,4-tetrahydroisoarsinolinium nitrate, 45
2-*p*-Hydroxyphenyl-2-phenyl-1,2,3,4-tetrahydroisophosphinolinium bromide, 12, 13
  optical resolution, 12
  d-camphor sulfonate, 12
9-Hydroxystibinafluorene anhydride, 132
Hypophosphorous acid, 85
  reaction with 10-chloro-5,10-dihydrophenarsazine, 85

I

Inductive deactivation, 124
Intervalency angles of
  arsenic atom, 108
  tertiary arsines, 108
  trialkyl antimony dihalides, 66, 67, 124
  tricyclic molecules, 108
6-Iodoarsa-1,2,3,4,-dibenzcyclohepta-1-3-diene, 58
9-Iodoarsafluorene, 38
2-Iodoarsaperinaphthane, 57
2-Iodobiphenyl, 52
  Grignard derivative, 52
1-Iodo-3-chloro-2(diethylaminomethyl)-arsindole hydriodide, 27
10-Iodo-5,10-dihydrostibacridine, 137
  Grignard derivative, 138
2-Iodoisoarsindoline, 34
10-Iodophenoxarsine, 101
o-(3-Iodopropylphenyl)dimethylarsine, 44
9-Iodostibinefluorene, 132
  Grignard derivative, 132
Isoarsindolines, 30, 31
  preparation and properties, 31, 32
  stability of ring structure, 34
"Isopropylacetonylphosphinic acid," 14

K

Kala azar, 152

L

Lewisite, 71
  reaction with 2,3-dithiolpropanol, 71

M

Mapharsen, 72
Matharside, 72
2-Mercaptoethanol, 96
Mesityl oxide, 14
10-Methoxy-5,10-dihydrophenarsazine, 82
  thermal decomposition, 83
o-(6′-Methoxy-2′-methyl-4′-quinolylamino)-phenylarsonic acid, 99
3-Methylarsacridinic acid, 51
9-Methylarsafluorene, 38
  methiodide, 38
1-Methylarsindole, 28
  mercurichloride, 28
  methiodide, 28
  picrate, 28
1-Methylarsindoline, 28, 31
  benzyl bromide derivative, 31
  ethiodide, 31
  methiodide, 31
  quaternary salts, dissociation, 31
N-Methylcarbazole, 38
1-Methylcyclopentamethylenearsine, 39
  dibromide, 40
  dichloride, 39
  di-iodide, 40
  methiodide, 39
  methopicrate, 39
  preparation and properties, 39
1-Methylcyclopentamethylenestibine, 135
  dichloride, 135
1-Methylcyclotetramethylenearsine, 26
  dichloride, 26
Methyldichloroarsine, 5, 39
  reaction with
    o-(2-bromoethyl)benzyl bromide and sodium, 45
    1,5-dibromopentane Grignard derivative, 39
    1,5-dichloro-*n*-hexane Grignard derivative, 39
    methyl iodide and aqueous sodium hydroxide, 5
Methyldichlorostibine, 135
10-Methyl-9,10-dihydroarsanthridine, 54
  methiodide, 54
  structure, 54, 55
10-Methyl-5,10-dihydrophenarsazine, 93
  dichloride, decomposition, 93
  methiodide, 93
  nitrosation, 94
10-Methyl-5,10-dihydrostibacridine, 138
  dibromide, 138
  dichloride, 138
  di-iodide, 138
4′-Methyldiphenylether-2-stibonic acid, 153
Methyl gallate, 145, 158
  reaction with
    antimony compounds, 145
    bismuth compounds, 158
2-Methylisoarsindoline, 34, 35
  reaction with *o*-xylylene dibromide, 35
10-Methyl-5-nitroso-5,10-dihydrophenarsazine, 94
5-Methylphenazarsinic acid, 91
10-Methylphenoxarsine, 106
  bromoacetic acid addition product, 106
  dihydroxide, 106
  methiodide, 106
10-Methylphenoxarsine-2-carboxylic acid, 108
  optical resolution, 109
  racemization in methyl iodide, 111
  strychnine salt, 109
2-Methylphenoxarsinic acid, 108
2-Methylphenoxstibines, 10-substituted, 155–156
Methyl-*o*-phenylbenzylchloroarsine, 54
  cyclization, 54
2-Methyl-1-phenylcyclopentamethylenearsine, 42
10-Methyl-10-phenyl-9,10-dihydroarsanthridinium iodide, 53
  absorption spectrum, 56
  picrate, 53
  stereochemistry, 54, 55
Methyl-2-phenylethylchloroarsine, 31
  cyclization, 31
2-Methyl-2-phenylisoarsindolinium iodide, 33
  picrate, 33
2-Methyl-10-phenylphenoxstibine, 153
  dichloride, 153
2-Methyl-10-phenylphenoxarsine, 112
Methyl(3-phenylpropyl)monobromoarsine, 43
Methyl(3-phenylpropyl)monochloroarsine, 43
  cyclization, 44

2-Methyl-2-phenyl-1,2,3,4-tetrahydroisophosphinolinium iodide, 11
9-Methylstibinafluorene, 132
  dibromide, 132
1-Methyl-1,2,3,4-tetrahydroarsinoline, 44
  dichloride, thermal dissociation, 44
  methiodide, dissociation in solution, 44
2-Methyl-1,2,3,4-tetrahydroisoarsinoline, 45
  dichloride, 46
  hydroxy nitrate, 45
  hydroxy picrate, 47
  methiodide, 47
  methopicrate, 47
  reaction with *o*-(2-bromoethyl)benzyl bromide, 48
Meyer reaction, 5

N

2-Naphthylamine, 88
  reaction with arsenic trichloride, 88
10-(1-Naphthyl)-5,10-dihydrophenarsazine, 93
o-Nitraniline, 88, 118
  use in Bart reaction, 88, 118
2-Nitrodiphenyl sulfide, 115
Nitrophenazarsinic acids, 84
2-Nitrophenazarsinic acid, 84
  normal and *aci* forms, 84
  reduction, 84
o-Nitrophenylarsonic acid, 118
5-Nitroso-10-phenyl-5,10-dihydrophenarsazine, 94
2-*p*-Nitrophenylethylamine, 141
o-Nitrophenyl-*p*-tolyl ether, 108
o-(5′-Nitro-8′-quinolylamino)-phenylarsonic acid, 94
  reduction and cyclization, 96
Nomenclature, 2

O

Oxamide, 16
Optical resolution of
  As-spiro-bis-1,2,3,4-tetrahydroisoarsinolinium bromide, 49
  3,4-benz-10-chloro-5,10-dihydrophenarsazine, 97
  10-*p*-carboxyphenyl-2-chlorophenoxarsine, 113
Optical resolution of (*continued*):
  10-*p*-carboxyphenyl-2-methylphenoxstibine, 154
  2-*p*-chlorophenacyl-2-phenyl-1,2,3,4-tetrahydroisoarsinolinium bromide, 48
  2-*p*-hydroxyphenyl-2-phenyl-1,2,3,4-tetrahydroisophosphinolinium bromide, 12
  10-ethylphenoxarsine-2-carboxylic acid and 10-methyl and 10-phenyl homologs, 108, 109, 112
  tripyrocatechylarsenic acid, 69

P

Palladium derivatives of tertiary arsines, 77
Pentamethylene dibromide, 10
  Grignard reagent, 10, 39, 134, 157, 162
Phenarsazines, 80, 82, 83. *See also* 5,10-Dihydrophenarsazine.
  acylation, 84
  alkyl and aryl derivatives, 93
  history, 87
  numbering, 80
  preparation and properties, 81, 83, 87, 88
  reduction, 85, 96
  reaction with Chloramine-T, 84
  structure, 85, 88
  therapeutic action, 81, 98
  use in chemical warfare, 98, 99
Phenarsazine chloride, 81
Phenarsazine oxide, 81, 101
Phenarsazine sulfide, 82
Phenarsazinic acid, 83. *See also* Phenazarsinic acid.
Phenazarsinic acids, 83, 88, 90, 96
  nitration, 83, 84
  reduction, 90
Phenazarsinous acids, 96
Phenoxarsines, 100
  numbering, 100
  physiological action, 101
  synthesis, 101, 105
  stereochemistry, 108, 109, 112
  structure, 102
Phenoxarsine oxide, 101
  reduction, 102
Phenoxarsine sulfide, 101

Phenoxarsinic acid, 101, 102
Phenoxstibines, 152
  numbering, 152
  synthesis, 153
  stereochemistry, 154
Phenphosphazines, 19
Phenphosphazinic acid, 21
  ethyl ester, 21
  methyl ester, 21
  nitro derivative, 21
  silver salt, 21
Phenthiarsine, 114
Phenylacetylene, 29
6-Phenylarsa-1,2,3,4-dibenzcyclohepta-1,3-diene, 58
  p-chlorophenacyl bromide derivative, 58
  methiodide, 58
    absorption spectrum, 56
2-Phenylarsaperinaphthane, 55
  methiodide, 57
    absorption spectrum, 56
  palladochloride, 57
  stability, 57
Phenylarsenoxide, 1, 62, 125
  formula, 1
  use in Bart reaction, 6, 118
1-Phenylarsindole, 28
Phenylarsinebis(magnesium bromide)
  reaction with
    2-biphenylylmethyl bromide, 53
    1,8-bis(bromomethyl)naphthalene, 55
    2,2′-dichlorodiethyl sulfide, 114
    o-xylylene dibromide, 32
Phenylarsonic acid, 1
  formula, 1
  sodium salt, 6
Phenylarsonous acid, 62
Phenyl-2-chlorovinylchloroarsine, 27
1-Phenylcyclopentamethylenearsine, 38, 39
  n-butyl iodide addition product, 42
  cyanogen bromide addition product, 42
  dichloride, 41
  ethiodide, 42
  isopropyl iodide addition product, 42
  mercurichloride, 41
  methiodide, 42
  preparation, 39, 41
  n-propyl iodide addition product, 42
1-Phenylcyclopentamethylenephosphine, 10
  ethiodide, 10
  mercuric chloride derivative, 10
1-Phenylcyclopentamethylenestibine, 134
  dichloride, 134
  oxide, 134
1-Phenylcyclotetramethylenearsine, 25
  dichloride, 25
  ethiodide, 26
  isopropyl iodide addition product, 26
  mercuric chloride derivative, 26
  methiodide, 26
  propyl iodide addition product, 26
1-Phenylcyclotetramethylenephosphine, 9
  ethiodide, 9
  mercuric chloride derivative, 9
  methiodide, 9
  n-propyl iodide derivative, 9
1-Phenylcyclotetramethylenestibine, 129
  dibromide, 130
  dichloride, 129
Phenyldichloroarsine, 1
  reaction with
    o-(2-bromoethyl)benzyl bromide, 45
    diphenylamine, 92
    diphenyl ether, 105
    di-*p*-tolylamine, 92
    Grignard reagent from
      pentamethylene dibromide, 39
      tetramethylene dibromide, 25
    lead pyrocatechol, 62
    phenylacetylene, 29
    phenyl-1-naphthylamine, 92
    phenyl-*p*-tolylamine, 92
    succinyl chloride, 26
    o-xylylene dibromide, 31
Phenyldichlorophosphinate, 14, 16
Phenyldichlorophosphine
  reaction with
    o-2-bromoethylbenzyl bromide, 11
    Grignard reagent from
      pentamethylene dibromide, 10
      tetramethylene dibromide, 9
Phenyldichlorostibine, 129, 134
Phenyldichlorothiophosphonate, 16
1-Phenyl-2(diethylaminomethyl)acetylene, 27
Phenyldihydrazinothiophosphinate, 17
  benzylidene derivative, 17

- 10-Phenyl-9,10-dihydroarsanthridine, 53
  - dibromopalladium derivative, 53
  - dichloropalladium derivative, 53
  - methiodide, absorption spectrum, 53, 56
  - methopicrate, 53
- 10-Phenyl-5,10-dihydrophenarsazine, 92, 93
  - dichloride, decomposition, 93
  - nitrosation, 94
- 10-Phenyl-5,10-dihydrostibacridine, 138
  - dichloride, 138
- Phenyldi-iodostibine, 153
  - reaction with 2,2′-dibromo-4-methyldiphenyl ether Grignard derivative, 153
- 1-Phenyl-2,5-diketo-cyclotetramethylenearsine, 26
  - ethiodide, 26
  - mercurichloride, 26
  - methiodide, 26
  - picrate, 26
- *o*-Phenylenebis(arsonous chloride) anhydride, 75
- *o*-Phenylenebis(di-*n*-butylarsine), 77
- *o*-Phenylenebis(di-*n*-butylarsine)dichloropalladium, 78
- *o*-Phenylenebis(dichloroarsine), 75
- *o*-Phenylenebis(dimethylarsine), 77, 80
  - reaction with
    - ethylene dibromide, 116
    - palladium salts, 77, 78
    - tin salts, 80
    - trimethylene dibromide, 127
- *o*-Phenylenebis(dimethylarsine)dichloropalladium, 78
- *o*-Phenylene bromostibinate, 144
- *o*-Phenylenechloromonothiophosphonate, 19
- *o*-Phenylenechlorophosphonate, 18
- *o*-Phenylenechlorophosphonites, 2, 17
- *o*-Phenylene chlorostibinate, 144
- *o*-Phenylenediamine, 15, 17, 94
  - reaction with
    - *o*-bromophenylarsonic acid, 94
    - phosphorus compounds, 15, 17
- *o*-Phenylenediarsonic acid, 75
- Phenylene-1,2-diphenylarsinic acid, 125
  - reduction, 125
- Phenylene-1,2-diphenylchloroarsine, 125
- *o*-Phenylene hydrogen stibinate, 143
  - derivatives with
    - alcohols and amines, 147
    - amino alcohols, 148
  - preparation and properties, 143
- *o*-Phenylene iodostibinate, 144
- *o*-Phenylenephenylarsonite, 62
- *o*-Phenylenetrimethylenediarsine, 127
- 2-Phenylethyl bromide, 30
  - Grignard derivative, 30
- Phenyl ethylenediaminophosphinate, 14
- Phenyl ethylenediaminothiophosphinate, 16
- 2-Phenylisoarsindoline, 32
  - dihydroxide, 33
  - homologs, 34
  - hydroxy nitrate, 33
  - hydroxy picrate, 33
  - methiodide, 33
  - preparation and properties, 32, 33
- 2-Phenylisoarsindoline oxide, 33
  - therapeutic action, 33, 34
- Phenyl-1-naphthylamine, 86
  - reaction with arsenic trichloride, 86
- Phenyl 1-naphthyl ether, 107
  - reaction with arsenic trichloride, 107
- 10-Phenylphenoxarsine, 106
  - methiodide, 107
  - oxide, 107
- 10-Phenylphenoxarsine-2-carboxylic acid, 112
  - optical resolution, 112
  - 1-phenylethylamine salt, 112
  - preparation, 112
- Phenyl-(2-phenyl-2-chlorovinyl)chloroarsine, 29
- Phenyl *o*-phenylenediaminophosphinate, 15
- Phenyl *o*-phenylenediaminothiophosphinate, 17
- Phenyl-(2-phenylvinyl)arsinic acid, 29
- Phenyl-(2-phenylvinyl) chloroarsine, 29
- 3-Phenylpropyl bromide, 43
  - Grignard derivative, 43
- 2-Phenyl-1,2,3,4-tetrahydroisoarsinoline, 45
  - *p*-chlorophenacyl bromide derivative, 47
  - hydroxy nitrate, 45, 47
  - hydroxy picrate, 47
  - methiodide, 47

2-Phenyl-1,2,3,4-tetrahydroisophosphinoline, 11
  methiodide, 11
Phenyl-thiarsine, 114
  mercuric chloride addition product, 114
  mercuric iodide addition product, 114
  methiodide, 114
2-Phenylvinyldichloroarsine, 28
Phosphinous acids, 2
  nomenclature, 2
Phosphonic acids, 2
  diamide and triamide, 14
  nomenclature, 2
Phosphorous acid, reaction with pyrocatechol, 17
Phosphorus, heterocyclic derivatives of, 9
Phosphorus oxychloride, structure, 4
Phosphorus trichloride
  reaction with
    acetone, 13
    ethylene glycol, 22, 23
Phthalamide, 16
Pinacol, 65, 66
  condensation with
    arsenic acid, 65
    arsinoacetic acid, 66
Potassium antimonyl tartrate, 140
  preparation and properties, 140
  structure, 140–143
Potassium gallate, 145
  reaction with antimony compounds, 145
Potassium phenyl sulfide, 114
  reaction with *o*-chloronitrobenzene, 115
Potassium pyridinotripyrocatechylantimonate, 149
Protocatechuic acid, 158
  bismuth derivatives, 158
Pyridine antimonyl tartrate, 142
Pyrido-5,10-dihydrophenarsazine, 96
Pyridophenarsazines, 96
Pyrocatechol
  derivatives of
    antimony, 143, 144, 148
    arsenic, 64, 67
    bismuth, 158, 159
    phosphorus, 17–19
  reaction with
    antimony pentoxide, 148
    antimony tribromide, 144
    antimony trichloride, 143, 144
Pyrocatechol, reaction with (*continued*):
    antimony trioxide, 146
    arsenic acid, 67
    arsinoacetic acid, 64
    bismuth salts, 158, 159
    phosphorus compounds, 17, 18, 19
Pyrocatechol-3,5-disulfonic acid, sodium salt, 147
  antimony derivative, 147
Pyrocatechyl antimonite, 143
Pyrocatechylchlorostibine, 144
Pyrocatechyl diacetate, 144
Pyrogallol, 144
  reaction with
    antimony trichloride, 144
    bismuth salts, 159
Pyrogallol-carboxylic acid, 159
  bismuth derivatives, 159

Q

Quaternary arsonium salts, 48, 49
  optical resolution, 48, 49
Quaternary phosphonium salts, 12
  optical resolution, 12

R

Ring Index, 9

S

Salicylchlorophosphonites, 21
Salicylic acid, 21
Salicyltrichlorophosphonate, 22
Schistosomiasis, 147, 152
Seven-membered ring systems
  containing
    only carbon and arsenic, 57
    carbon and two arsenic atoms, 127
Silicon, heterocyclic derivatives, 161
Silicon tetrachloride, 161
Six-membered ring systems
  containing
    only carbon and antimony, 134
    only carbon and arsenic, 38
    only carbon and bismuth, 157
    only carbon and phosphorus, 10
    only carbon and silicon, 161
    carbon, antimony, and oxygen, 152
    carbon and two arsenic atoms, 116
    carbon, arsenic, and nitrogen, 80

Six-membered ring systems, containing (*continued*):
    carbon, arsenic, and oxygen, 100
    carbon, arsenic, and sulfur, 114
    carbon, phosphorus, and nitrogen, 19
    carbon, phosphorus, and oxygen, 21
Sodium antimonyl tartrate, 145
  reaction with 1,2-dihydric phenols, 145
Sodium methyl-arsonate, 5
Sodium pyridinotripyrocatechyl antimonate, 149
Spirochetocidal action, 73
  of BAL–matharside condensation product, 73
Spirocyclic arsonium salts, 35, 36
  optical resolution, 49
  preparation, 35, 49
Spirocyclic diarsine palladium compounds, 79
Spirocyclic esters of
    o-dihydroxybenzenes with arsonic acids, 62
    glycols with arsonic acids, 62
    α-hydroxycarboxylic acids with arsonic acids, 62
Stereochemistry of
  arsanthrene derivatives, 121
  As-spiro-bis-1,2,3,4-tetrahydroisoarsinolinium salts, 49
  3,4-benz-10-chloro-5,10-dihydrophenarsazine, 97
  3-covalent arsenic atom, 108
  5,10-dichloro-5,10-dihydroarsanthrene, 122
  9,10-dihydroarsanthridine ring system, 54, 55
  5,10-di-*p*-tolyl-5,10-dihydroarsanthrene, 122
  ethylene-1,2-bis(*n*-butylphenylarsine)-dichloropalladium, 78
  ethylene-1,2-bis(*n*-butylphenylarsine sulfide), 78
  phenoxarsines, 108, 109, 110
  phenoxstibines, 154
  quaternary arsonium salts, 36, 49
  quaternary phosphonium salts, 12
  1,2,3,4-tetrahydroisoarsinolines, 47
  1,2,3,4-tetrahydroisophosphinolines, 12
  tricyclic molecules, 108
  trimethylstibine dihalides, 66
  tripyrocatechylarsenic acid, 69
Stibacridines, 135
  nomenclature, 136
  numbering, 135
10-Stibina-anthracene, 136
2-Stibina-1,3-dithiacyclopentanes, 150
  numbering, 150
  preparation and properties, 150
Stibinafluorenes, 130
  nomenclature, 130
  numbering, 130
  synthesis, 131
Stibine dihalides, 66
  structure, 66
Stibinous acids, 131
  nomenclature, 2
Stibonic acids, 2
  nomenclature, 2
10-Substituted-5,10-dihydrophenarsazines, 51. *See* Phenarsazines.
5-Substituted 5,10-dihydrophenphosphazines, 19
10-Substituted 5,10-dihydrostibacridines, 136
  preparation and properties, 136
2-Substituted isoarsindolines, 31
  stability, 34
  table, 34
10-Substituted 2-methylphenoxstibines, 155–156
  table, 156
10-Substituted phenoxstibines, 152
  stereochemistry, 154
  synthesis, 153
Succinamide, 16
Succinyl chloride, 26
Succinylphenylarsine, 26
Symbols, use of, 4

T

Tartar emetic, 140. *See also* Potassium antimonyl tartrate.
d-Tartaric acid, 66
  condensation with arsinoacetic acid, 66
Ten-membered ring systems containing carbon, phosphorus, and oxygen, 22
Tertiary arsines
  palladium derivatives, 77
  preparation, 5
  tin derivatives, 80
Tertiary arsine dichlorides, 66
  structure, 66

Tertiary arsine dihydroxides, 66
Tertiary arsine oxides, 5
  reduction, 5
Tertiary stibine dihalides, 66, 124
  structure, 66
Tetra-aryl arsonium salts, 70
  attempted optical resolution, 70
Tetrachloro[*o*-phenylenebis(dimethylarsine)]tin, 80
1,2,3,4-Tetrahydroarsinolines, 42, 43
  numbering, 42
  preparation and properties, 43, 44
  stability of ring system, 44
1,2,3,4-Tetrahydrophosphinolines, 13
Tetrahydroquinoxaline, 116
Tetramethylene dibromide, 9
  Grignard reagent, 9, 25, 129
1,1,4,4-Tetramethylethylene-*o*-phenylenediarsonium dibromide, 116
  dipicrate, 117
1,2,3,4-Tetrahydroisoarsinolines, 42, 45
  numbering, 42
  preparation, 45
  stability of ring system, 45
  stereochemistry of quaternary salts, 48, 49
1,2,3,4-Tetrahydroisophosphinolines, 10
1,2,3,4-Tetrahydroisoquinoline, 10, 42
1,2,3,4-Tetrahydroquinoline, 42
Therapeutic action of
  adamsite, 98
  antimonyl thioglycollate, sodium salt, 152
  antimonyl tartrates, 143
  arsindoles, 28
  BAL–matharside condensation product, 73
  10-*p*-carboxyphenyl-2-methylphenoxstibine, 156
  10-chloro-5,10-dihydrophenarsazine, 81, 98
  dithiols, 71
  fuadin, 147
  4-hydroxymethyl-2(3′-amino-4′-hydroxyphenylarsa)-1,3-dithiacyclopentane and its hydrochloride, 73
  matharside, 73
  phenarsazines, 81, 98
  phenoxarsines, 101
  phenoxstibines, 156
  2-phenylisoarsindoline oxide, 33, 34
  pyrocatechol-3,5-disulfonic acid, sodium antimony derivative, 147
  tartar emetic, 143
1-Thiocyanatocyclopentamethylenearsine, 39
10-Thiocyanatophenoxarsine, 101
Thioglycollic acid, 151
  derivatives of antimony and arsenic, 151
  ethyl ester, 152
    reaction with antimony trioxide, 152
  reaction with
    antimony trichloride, 151
    antimony trioxide, 151
    2-chloroarsa-1,3-dithiacyclopentane, 75
    2-chlorostibina-1,3-dithiacyclopentane, 150
Thiol-lactic acid, 152
  reaction with antimony trichloride, 152
m-Thiolbenzoic acid, 150
  reaction with 2-chlorostibina-1,3-dithiacyclopentane, 150
1-*p*-Tolylcyclopentamethylenearsine, 42
  dichloride, 42
  mercurichloride, 42
1-*p*-Tolylcyclopentamethylenephosphine, 10
  ethiodide, 10
  mercuric chloride derivative, 10
p-Tolyldichlorophosphine, 10, 11
p-Tolyldichlorophosphine oxide, 19
p-Tolyl ethylenediaminophosphinate, 15
2-*p*-Tolylisoarsindoline, 34
  hydroxy nitrate, 34
  hydroxy picrate, 34
  methiodide, 34
  methopicrate, 34
  oxide, 34
2-(*p*-Tolyloxyphenyl)arsonic acid, 108
  cyclization, 108
p-Tolyl *o*-phenyldiaminothiophosphinate, 17
p-Tolylphosphonic acid, 19
  o-phenylene ester, 19
2-*p*-Tolyl-1,2,3,4-tetrahydroisophosphinoline, 11
  p-chlorophenacyl bromide derivative, 11
1,1,1-Tribromocyclopentamethylenearsine, 41

10,10,10-Trichloro-5,10-dihydrostibacridine, 137
Trichomonacidal action, 73
  of matharside, 73
Tri(ethylenedioxy)arsenic acid, 65
  aniline salt, 65
  brucine salt, 65
  pyridine salt, 65
2,3,4-Trihydroxybenzaldehyde, 145
  reaction with sodium antimonyl tartrate, 145
3,4,5-Trihydroxybenzoylglycollic acid, 145
  reaction with sodium antimonyl tartrate, 145
Trimethylarsine oxide, 5
  preparation by Meyer reaction, 5
Trimethylene dibromide, 127
2,10,10-Trimethylphenoxarsonium iodide, 111
Trimethylstibine dihalides, 66, 67, 124
  structure, 66
Triphenarsazine amine, 82
Triphenarsazine chloride, 82
Triphenylarsine
  dichloride, 1
  formula, 1
  oxide, 1
Tri-*o*-phenylenediarsine and derivatives, 118, 125
  dioxide, 126
  preparation, 118, 126
  tetrabromide, 126
    thermal decomposition, 127
Tri-*o*-phenylene diphosphate, 18
Tri-*o*-phenylene diphosphite, 17
Tri(2-phthalimidoethyl)amine, 82
Tripyrocatechylarsenic acid, 67, 149
  optical resolution, 69
  preparation and properties, 67, 68
  salts, 69
  structure, 68
Tripyrocatechylantimonic acid, 148
  structure and properties, 149
Tris(2-phenylvinyl)arsine, 28
Trypanocidal action of
  BAL–matharside condensation product, 73
  10-*p*-carboxyphenyl-2-methylphenoxstibine, 156
  2-phenylisoarsindoline oxide, 33, 34
Tripyrocatechylarsenic acid, 67

U

Urea, 21
  reaction with phosphorus pentasulfide, 21

V

o-Vinylphenyldichloroarsine, 27

X

Xenylamines, 130
Xenylenestibine chloride, 130
Xenylene radicals, 130
Xenyl radicals, 130
o-Xylylene arsinic acid, 35
  dihydroxy nitrate, 35
o-Xylylene dibromide
  reaction with
    dimethylphenylarsine, 32
    2-methylisoarsindoline, 35
    phenylarsine Grignard derivative, 32
    phenyldichloroarsine, 31

DATE OF ISSUE

15 APR 1961

This book must be returned within 3,7,14 days of its issue. A fine of ONE ANNA per day will be charged if the book is overdue.